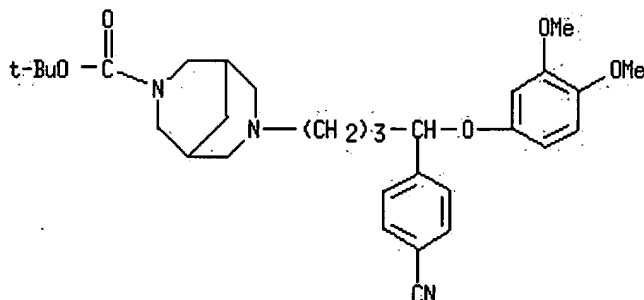


Session text above this point is available in the transcript,
available from the **Transcript Assistant** on the toolbar.

use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bispidines useful in the treatment of cardiac
arrhythmias)

RN 312955-28-5 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[4-(4-cyanophenyl)-4-(3,4-dimethoxyphenoxy)butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:

2000:720062 HCAPLUS

DOCUMENT NUMBER:

134:51214

TITLE:

Comparative effects of azimilide and ambasilide on the human ether-a-go-go-related gene (HERG) potassium channel

AUTHOR(S):

Walker, B. D.; Singleton, C. B.; Tie, H.; Bursill, J. A.; Wyse, K. R.; Valenzuela, S. M.; Breit, S. N.; Campbell, T. J.

CORPORATE SOURCE:

Department of Medicine, University of New South Wales and Victor Chang Cardiac Research Institute, St Vincent's Hospital, Sydney, Australia

SOURCE:

Cardiovascular Research (2000), 48(1), 44-58

CODEN: CVREAU; ISSN: 0008-6363

PUBLISHER:

Elsevier Science B.V.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Objective: To evaluate the effects of azimilide and ambasilide on the biophys. properties of the human-ether-a-go-go-related (HERG) channel. Methods: HERG was stably transfected into Chinese hamster ovary (CHO-K1) cells and currents were measured using a whole cell, voltage-clamp technique. Results: Azimilide had a 'dual effect', inhibiting current at voltage steps above -40 mV and augmenting current at -40 and -50 mV. Tail current inhibition following a step to +30 mV did not vary with temp. (IC50 610 nM at 22 and 560 nM at 37). The agonist effect at -50 mV was concn.-dependent and correlated with a hyperpolarizing shift in the V1/2 of activation (r=0.98, P<0.05). Time consts. of inactivation were faster and there was a -10 mV shift in the V1/2 of steady state inactivation suggestive of open and inactivated state binding. By comparison, ambasilide inhibited HERG channels with lower potency (IC50 3.6 μM), in a voltage- and time-dependent but frequency-independent manner (0.03-1

Hz). Ambasilide had no effect on activation or inactivation gating but prolonged both fast and slow components of deactivation consistent with unbinding from the open state. The net effect of both drugs was similar during a voltage ramp which simulated a cardiac action potential. Conclusions: Inhibition of HERG channels by azimilide and ambasilide exhibits a similar time and voltage-dependence. While both exhibit affinity for the open state, azimilide also binds to inactivated channels.

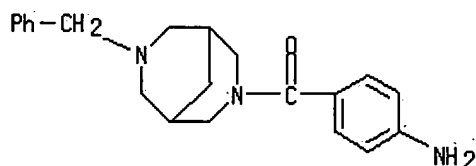
IT 83991-25-7, Ambasilide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(comparative effects of azimilide and ambasilide on human ether-a-go-go-related gene (HERG) potassium channel and **antiarrhythmic** activity)

RN 83991-25-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
(CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2000:622035 HCAPLUS

DOCUMENT NUMBER: 133:317402

TITLE: Analysis of the electrophysiological effects of ambasilide, a new **antiarrhythmic** agent, in canine isolated ventricular muscle and Purkinje fibers

AUTHOR(S): Balati, B.; Iost, N.; Simon, J.; Varro, A.; Papp, J. G.

CORPORATE SOURCE: Department of Pharmacology and Pharmacotherapy, Research Unit for Cardiovascular Pharmacology, Hungarian Academy of Science, Albert Szent-Gyorgyi Medical University, Szeged, H-6701, Hung.

SOURCE: General Pharmacology (2000), 34(2), 85-93
CODEN: GEPHDP; ISSN: 0306-3623

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of the study was to det. the in vitro rate-dependent cellular electrophysiol. effects of ambasilide (10 and 20 $\mu\text{M/l}$), a new investigational **antiarrhythmic** agent, in canine isolated ventricular muscle and Purkinje fibers by applying the std. microelectrode technique. At the cycle length (CL) of 1000 ms, ambasilide significantly prolonged the action potential duration measured at 90% repolarization (APD90) in both ventricular muscle and Purkinje fibers. Ambasilide (10 $\mu\text{M/l}$) produced a more marked prolongation of APD90 at lower stimulation frequencies in Purkinje fibers (at CL of 2000 ms = $56.0 \pm 16.1\%$, $n = 6$, vs. CL of 400 ms = $15.1 \pm 3.7\%$, $n = 6$; $p < 0.05$), but, in 20 $\mu\text{M/l}$, this effect was considerably diminished ($15.2 \pm 3.6\%$, $n = 6$, vs. $7.3 \pm 5.1\%$, $n = 6$, $p < 0.05$). In ventricular muscle, however, both

concns. of the drug induced an almost frequency-independent lengthening of APD90 in response to a slowing of the stimulation rate (in 20 $\mu\text{M/l}$ at CL of 5000 ms = $19.0 \pm 1.5\%$, $n = 9$, vs. CL of 400 ms = $16.9 \pm 1.4\%$, $n = 9$). Ambasilide induced a marked rate-dependent depression of the maximal rate of rise of the action potential upstroke (V_{max}) (in 20 $\mu\text{M/l}$ at CL of 300 ms = $-45.1 \pm 3.9\%$, $n = 6$, vs. CL of 5000 ms = $-8.5 \pm 3.9\%$, $n = 6$, $p < 0.05$, in ventricular muscle) and the corresponding recovery of V_{max} time const. was $\tau = 1082.5 \pm 205.1$ ms ($n = 6$). These data suggest that ambasilide, in addn. to its Class III **antiarrhythmic** action, which is presumably due to its inhibitory effect on the delayed rectifier potassium current, possesses I/B type **antiarrhythmic** properties as a result of the inhibition of the fast sodium channels at high frequency rate with relatively fast kinetics. This latter effect may play an important role in its known less-pronounced **proarrhythmic** ("torsadogenic") potential.

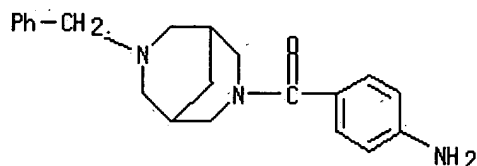
IT 83991-25-7, Ambasilide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(electrophysiol. effects of ambasilide, a new **antiarrhythmic** agent, in canine isolated ventricular muscle and Purkinje fibers)

RN 83991-25-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
(CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2000:260016 HCAPLUS

DOCUMENT NUMBER: 132:284247

TITLE: A dried or frozen pharmaceutical preparation containing a class III **antiarrhythmic** compound

INVENTOR(S): Bjore, Annika; Granath, Anna-Karin

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021533	A1	20000420	WO 1999-SE1828	19991011
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,				

AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2315375	AA	20000420	CA 1999-2315375	19991011
BR 9906869	A	20001017	BR 1999-6869	19991011
EP 1043997	A1	20001018	EP 1999-970322	19991011

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO

EE 200000354	A	20011217	EE 2000-354	19991011
JP 2002527394	T2	20020827	JP 2000-575509	19991011
US 6492382	B1	20021210	US 1999-423200	19991103
ZA 2000002749	A	20010111	ZA 2000-2749	20000601
NO 2000002986	A	20000609	NO 2000-2986	20000609

PRIORITY APPLN. INFO.:

SE 1998-3517	A	19981015
WO 1999-SE1828	W	19991011

OTHER SOURCE(S): MARPAT 132:284247

AB The present invention relates to dried preps. contg. a class III antiarrhythmic compd. in the form of cryst. or amorphous salt or any combination thereof, where the counterion is selected from pharmaceutically acceptable water-sol. org. or inorg. acids. The present invention also relates to frozen preps. contg. a class III antiarrhythmic compd. in the form of salt soln., where the counterion is selected from pharmaceutically acceptable water-sol. org. or inorg. acids. Preferred preps. contain a salt of the compd. 3,7-diazabicyclo[3.3.1]nonane-3-carboxylic acid 7-[(2S)-3-(4-cyanophenoxy)-2-hydroxypropyl]-1,1-dimethylethyl ester (Compd. A). Further aspects of the present invention include salts of Compd. A per se, processes for prepg. the prepn., as well as use of the preps. for prophylaxis and/or treatment of cardiac arrhythmia.

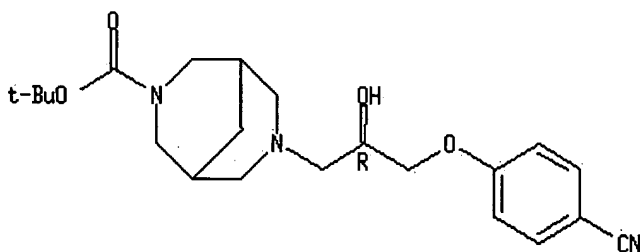
IT 227940-01-4

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); THU (Therapeutic use); THU (Therapeutic use); USES (Uses)
 (freeze-dried pharmaceuticals contg. antiarrhythmic diazabicyclononanecarboxylate deriv.)

RN 227940-01-4 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[(2R)-3-(4-cyanophenoxy)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2000:211822 HCAPLUS

DOCUMENT NUMBER: 132:343051

TITLE: Effect of GLG-V-13, a class III **antiarrhythmic** agent, on potassium currents in rabbit ventricular myocytes

AUTHOR(S): Virag, Laszlo; Fazekas, Tamas; Iost, Norbert; Varro, Andras; Berlin, K. Darrell; Scherlag, Benjamin J.; Lazzara, Ralph; Papp, Julius Gy.

CORPORATE SOURCE: Department of Pharmacology and Pharmacotherapy, Albert Szent-Gyorgyi Medical University, Szeged, H-6701, Hung.

SOURCE: Life Sciences (2000), 66(17), PL253-PL258
CODEN: LIFSAK; ISSN: 0024-3205

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of a new Class III **antiarrhythmic** drug, GLG-V-13, on the 4-aminopyridine sensitive transient outward current, on the inward rectifier potassium current, on the ATP sensitive potassium current and on the rapid and slow components of the delayed rectifier potassium current were studied in single rabbit ventricular myocytes using the whole-cell voltage-clamp technique. GLG-V-13 blocked the rapid component of the delayed rectifier potassium current in a dose-dependent manner, with an estd. EC50 value of 0.36 μ M. At high concn., the slow component of the delayed rectifier potassium current was also depressed by the drug (40% effect at 10 μ M concn.). The transient outward current, the inward rectifier potassium current and the ATP sensitive potassium current were not influenced by GLG-V-13, even at 10 μ M concn. Thus, GLG-V-13 blocks predominantly the rapid component of the delayed rectifier potassium current which may play a significant role in the prolongation of repolarization by the drug in ventricular tissue.

IT 155029-33-7, GLG-V-13

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(effect of GLG-V-13, a class III **antiarrhythmic** agent, on potassium currents in rabbit ventricular myocytes)

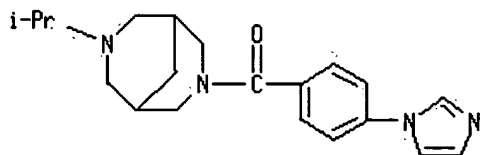
RN 155029-33-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-[4-(1H-imidazol-1-yl)benzoyl]-7-(1-methylethyl)-, diperchlorate (9CI) (CA INDEX NAME)

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CRN 155029-32-6

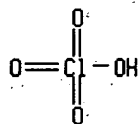
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CRN 7601-90-3

CMF Cl H O4



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2000:187936 HCAPLUS
 DOCUMENT NUMBER: 133:12555
 TITLE: Effects of ambasilide, quinidine, flecainide and verapamil on ultra-rapid delayed rectifier potassium currents in canine atrial myocytes
 AUTHOR(S): Yue, L.; Feng, J. L.; Wang, Z.; Nattel, S.
 CORPORATE SOURCE: Montreal Heart Institute and Research Center, Department of Medicine, Department of Pharmacology and Therapeutics, McGill University, University of Montreal, Montreal, QC, Can.
 SOURCE: Cardiovascular Research (2000), 46(1), 151-161
 CODEN: CVREAU; ISSN: 0008-6363
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

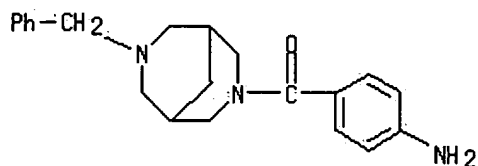
AB Objective: A dog atrial ultra-rapid delayed rectifier current (IKur.d) is involved in canine atrial repolarization and shares similarities with the human atrial ultra-rapid delayed rectifier (IKur). Almost no information is available about the actions of **antiarrhythmic** drugs on IKur.d. This study evaluated effects of ambasilide, quinidine, flecainide and verapamil on IKur.d in isolated canine atrial myocytes. Methods: Std. whole-cell patch clamp techniques were used to study the effects of multiple concns. of each drug. Results: All drugs produced reversible concn.-, voltage- and time-dependent IKur.d inhibition. Significant effects of quinidine, flecainide and ambasilide were noted at atrial-effective **antiarrhythmic** concns. in the dog. Upon the onset of a depolarizing pulse, block developed exponentially in relation to time, with the blocking rate-const. increasing with drug concn., consistent with open-channel blockade and permitting the calcn. of forward and reverse rate-consts. For all drugs, the 50% blocking concn. (EC50) showed significant voltage-dependence, decreasing at more pos. potentials. The magnitude of voltage-dependent block was directly related to the degree of drug-induced shift in the voltage dependence of activation (r=0.97), pointing to open-channel block as a mechanism for voltage-dependent action. An addnl. component of voltage-dependence suggested that blocking sites were subjected to 17-21% of the transmembrane voltage field. Conclusions: Ambasilide, quinidine, flecainide and verapamil inhibit IKur.d, with preferential action on the open state. IKur.d inhibition may play a role in **antiarrhythmic** effects in canine atrial **arrhythmia** models. Comparisons between the effects of these drugs on IKur.d and previously studied effects on IKur suggest potential opportunities for investigating the mol. structural determinants of drug-blocking action on atrial-specific ultrarapid delayed rectifiers.

IT 83991-25-7, Ambasilide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**antiarrhythmics** ambasilide, quinidine, flecainide and verapamil effect on ultra-rapid delayed rectifier potassium currents in atrial myocytes)

RN 83991-25-7 HCAPLUS
 CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
 (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:	2000:114187 HCAPLUS
DOCUMENT NUMBER:	132:231737
TITLE:	Preliminary acute and subchronic toxicity studies of GLG-V-13, a novel class III antiarrhythmic agent, in mice
AUTHOR(S):	Chen, Chun-Lin; Chandra, Sundeep A. M.; Kim, Soochong; Sangiah, Subbiah; Chen, Hao; Roder, Joseph D.; Qualls, Charles W., Jr.; Garrison, Gregory L.; Cowell, Rick L.; Berlin, Kenneth D.; Scherlag, Benjamin J.; Lazzara, Ralph
CORPORATE SOURCE:	Department of Anatomy, Pathology and Pharmacology, Oklahoma State University, Stillwater, OK, USA
SOURCE:	Arzneimittel-Forschung (2000), 50(1), 31-38 CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER:	Editio Cantor Verlag
DOCUMENT TYPE:	Journal
LANGUAGE:	English
AB	The acute and subchronic toxic effects of GLG-V-13 (3-[4-(1H-imidazol-1-yl)benzoyl]-7-isopropyl-3,7-diazabicyclo[3.3.1]nonane dihydroperchlorate, CAS 155029-33-7), a novel class III with some class Ib antiarrhythmic activity, were investigated in mice. The estd. LD50 for GLG-V-13 given orally were 419 mg/kg for male mice and 383 mg/kg for female mice, resp. The acute toxic signs appeared to be of the central nervous system in origin. 4 Groups of mice (15 per sex, group, and dose) were fed daily with diets contg. GLG-V-13 for 90 consecutive days. The equivalent daily doses were 0, 22, 50, and 121 mg/kg/day and 0, 27, 60, and 136 mg/kg/day for male and female mice, resp. All of the mice survived. Food consumption was decreased. However, mean body wt. and body wt. gain were not changed. Gross pathol. changes, esp. in the lungs and liver, were found in the middle and high dose groups. Consistent increased mean corpuscular Hb concn. and decreased mean corpuscular Hb were obsd. in all dose groups. Hepatocellular necrosis was found in both male and female mice treated with the drug and was dose-dependent. Marked vacuolation of the X zone in the adrenal gland with mild to moderate deposition of ceroid pigments (brown degeneration) was obsd. in female mice. Lesions in the kidneys and adrenal glands may be a possible reason for changes in blood serum Na and K ions concns. leading to an increase in water intake. A redn. in cholesterol in the high dose group may be a favorable pharmacol. effect of GLG-V-13. The data from the 90-day subchronic toxicity studies indicate that GLG-V-13 appears to have limited systemic toxicity potential.
IT	155029-33-7, GLG-V-13
	RL: ADV (Adverse effect, including toxicity); THU (Therapeutic

use); BIOL (Biological study); USES (Uses)
(acute and subchronic toxicity of GLG-V-13)

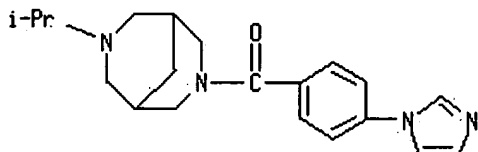
RN 155029-33-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-[4-(1H-imidazol-1-yl)benzoyl]-7-(1-methylethyl)-, diperchlorate (9CI) (CA INDEX NAME)

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CRN 155029-32-6

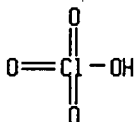
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CM 2

CRN 7601-90-3

CMF Cl H O4



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1999:795686 HCAPLUS

DOCUMENT NUMBER: 132:35505

TITLE: Novel multibinding potassium channel drugs and their uses

INVENTOR(S): Jacobsen, John R.; Eastman, Donna; Griffin, John H.

PATENT ASSIGNEE(S): Advanced Medicine, Inc., USA

SOURCE: PCT Int. Appl., 175 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 31

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964050	A1	19991216	WO 1999-US12777	19990607
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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<u>CA 2318806</u>	AA	19991216	<u>CA 1999-2318806</u> 19990607
<u>CA 2319142</u>	AA	19991216	<u>CA 1999-2319142</u> 19990607
<u>CA 2319153</u>	AA	19991216	<u>CA 1999-2319153</u> 19990607
<u>WO 9963984</u>	A1	19991216	<u>WO 1999-US11801</u> 19990607
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<u>WO 9963932</u>	A3	20000203	
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<u>WO 9964045</u>	A1	19991216	<u>WO 1999-US12754</u> 19990607
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
<u>AU 9944264</u>	A1	19991230	<u>AU 1999-44264</u> 19990607
<u>AU 9945511</u>	A1	19991230	<u>AU 1999-45511</u> 19990607
<u>AU 9946726</u>	A	19991230	<u>AU 1999-46726</u> 19990607
<u>EP 1086063</u>	A1	20010328	<u>EP 1999-927330</u> 19990607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
<u>EP 1085879</u>	A2	20010328	<u>EP 1999-928442</u> 19990607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
<u>EP 1085890</u>	A1	20010328	<u>EP 1999-930122</u> 19990607
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<u>EP 1089749</u>	A1	20010411	<u>EP 1999-928447</u> 19990607
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<u>JP 2002517437</u>	T2	20020618	<u>JP 2000-553053</u> 19990607
<u>JP 2002517466</u>	T2	20020618	<u>JP 2000-553118</u> 19990607
<u>SG 80037</u>	A1	20010417	<u>SG 1999-2714</u> 19990608
<u>ZA 2000004562</u>	A	20011130	<u>ZA 2000-4562</u> 20000831
<u>ZA 2000004563</u>	A	20011130	<u>ZA 2000-4563</u> 20000831
<u>ZA 2000004564</u>	A	20011130	<u>ZA 2000-4564</u> 20000831
<u>US 2003044845</u>	A1	20030306	<u>US 2002-75017</u> 20020213
PRIORITY APPLN. INFO.:			
		<u>US 1998-88465P</u>	P 19980608
		<u>US 1998-93068P</u>	P 19980716

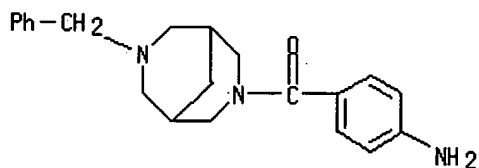
US 1998-113864P P 19981224
 US 1999-327096 B1 19990607
 WO 1999-US11801 W 19990607
 WO 1999-US12724 W 19990607
 WO 1999-US12754 W 19990607
 WO 1999-US12777 W 19990607
 US 2000-499176 B1 20000207

AB This invention relates to novel multibinding compds., LpXq [where L = a ligand capable of binding to a K⁺ channel; X = a linker; p = 2-10; q = 1-20], that bind to potassium (K⁺) channels and modulate their activity. Combinatorial arrays, methods of synthesis, and methods of assaying the dimeric and multimeric compds. are also embodied by the invention. A no. of divalent prophetic examples for compds. contg. two aryl ligands and a difunctional linker are given. Compds. of this invention are useful in the treatment of diseases and conditions of mammals that are mediated by K⁺ channels, such as diabetes, hypertension, and **arrhythmia** (no data). The claimed multibinding compds., which combine a K⁺ channel opener with little or no effect on cardiac action potential and a Class III **antiarrhythmic** compd., provide greater biol. and/or therapeutic effects than the aggregate of the unlinked ligands due to their multibinding properties (no data). Ligands may include quinidine, glibenclamide, procaine, tetra-Et ammonium, clofilium, melperone, pinacidil, WAY-123398, cromakalim, propofol, thiopentone, risotilide, almokalant, bretylium, N-acetylprocainamide, tacrine, UK66914, RP58866, 4-aminopyridine, RP49356, alinidine, chromanol 293B, L-768673 and its analogs, bethanidine, disopyramide, desethylamiodarone, NE-10064, artilide, dofetilide, E-4031, sematilide, ambasilide, azimilide, tedisamil, dronedarone, ibutilide, sotalol, benzodiazepine analogs, and amiodarone.

IT **83991-25-7DP**, Ambasilide, dimeric and multimeric derivs. of
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
 (target compd.; prepn. of multibinding K⁺ channel drugs as antidiabetics, antihypertensives, and **antiarrhythmics**)

RN **83991-25-7** HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
 (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 18 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1999:476866 HCAPLUS

DOCUMENT NUMBER: 131:237731

TITLE: Chronotropic, inotropic, dromotropic and coronary vasodilator effects of bisaramil, a new class I **antiarrhythmic** drug, assessed using canine isolated, blood-perfused heart preparations

AUTHOR(S): Haruno, Akihiro; Sugiyama, Atsushi; Hashimoto, Keitaro

CORPORATE SOURCE: Department of Pharmacology, Yamanashi Medical University, Yamanashi, 409-3898, Japan

SOURCE: Japanese Journal of Pharmacology (1999), 80(3), 267-270
 CODEN: JJPAAZ; ISSN: 0021-5198
 PUBLISHER: Japanese Pharmacological Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The cardiovascular effects of a new class I **antiarrhythmic** drug, bisaramil, were examd. using canine isolated, blood-perfused heart preps. Bisaramil exerted neg. chronotropic, inotropic and dromotropic effects as well as coronary vasodilator action, which are qual. the same as those of classical class I drugs. The selectivity of bisaramil for the intraventricular conduction vs. the other cardiac variables was compared with that of disopyramide and flecainide. Bisaramil was the most selective for intraventricular conduction, while it was the least selective for ventricular muscle contraction. The authors conclude that bisaramil may become a useful **antiarrhythmic** drug with less cardiac adverse effects.

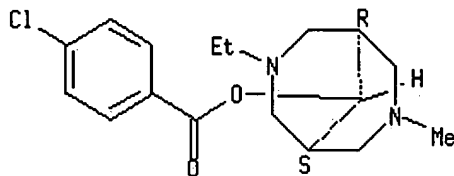
IT 89194-77-4, Bisaramil

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU** (Therapeutic use); BIOL (Biological study); USES (Uses)
 (chronotropic and inotropic and dromotropic and coronary vasodilator effects of bisaramil as new class I **antiarrhythmic** drug assessed using canine isolated and blood-perfused heart preps. in relation to adverse effects)

RN 89194-77-4 HCAPLUS

CN Benzoic acid, 4-chloro-, (9-syn)-3-ethyl-7-methyl-3,7-diazabicyclo[3.3.1]non-9-yl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1999:404964 HCAPLUS

DOCUMENT NUMBER: 131:58860

TITLE: Preparation of 3,7-diazabicyclo[3.3.1]nonane-3-carboxylates as **antiarrhythmic** agents

INVENTOR(S): Strandlund, Gert; Alstermark, Christer; Bjore, Annika; Bjorsne, Magnus; Frantsi, Marianne; Halvarsson, Torbjorn; Hoffmann, Kurt-Jurgen; Lindstedt, Eva-Lotte; Polla, Magnus

PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.

SOURCE: PCT Int. Appl., 129 pp.
 CODEN: PIXXD2

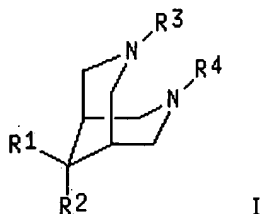
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931100	A1	19990624	WO 1998-SE2276	19981210
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9811130	A	19990617	ZA 1998-11130	19981204
CA 2314490	AA	19990624	CA 1998-2314490	19981210
AU 9917953	A1	19990705	AU 1999-17953	19981210
BR 9813668	A	20001017	BR 1998-13668	19981210
EP 1047695	A1	20001102	EP 1998-962796	19981210
EP 1047695	B1	20040317		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EE 200000365	A	20011015	EE 2000-200000365	19981210
JP 2002508375	T2	20020319	JP 2000-539024	19981210
US 6291475	B1	20010918	US 1999-214756	19990112
NO 2000003137	A	20000817	NO 2000-3137	20000616
PRIORITY APPLN. INFO.:			SE 1997-4709	A 19971217
			WO 1998-SE2276	W 19981210
OTHER SOURCE(S): MARPAT 131:58860				
GI				



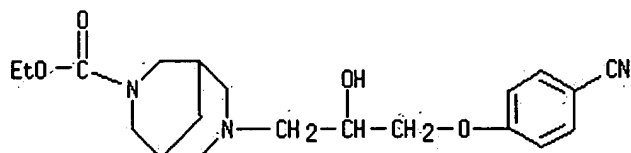
AB Title compds. [I; R1,R2 = H or alkyl; R1R2 = OCH2CH2O, (CH2)4-5; R3 = CCR10R11AR; A = bond, alkylene, (CH2)nZ, CONR20, etc.; B = bond, alkylene, NR23(CH2)r, O(CH2)r; R = (un)substituted Ph; R4 = COXR9; R9 = alkyl, (un)substituted phenyl(alkyl), -naphthyl; R10 = H or OH; R11,R20,R23 = H or alkyl; X = O or S; Z = NR20, SO0-2, O; n,r = 0-4] were prepd. Thus, 4-(NC)C6H4OH was condensed with epichlorohydrin and the product aminated by I (R1 = R2 = H, R4 = CO2CMe3) (II; R3 = H) (prepn. given) to give II [R3 = CH2CH(OH)CH2OC6H4(CN)-4]. Data for biol. activity of I were given.

IT **227939-98-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of 3,7-diazabicyclo[3.3.1]nonane-3-carboxylates as **antiarrhythmic agents**)

RN 227939-98-2 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[3-(4-cyanophenoxy)-2-hydroxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:	1999:275333 HCAPLUS
DOCUMENT NUMBER:	131:67881
TITLE:	Ambasilide prolongs the action potential and blocks multiple potassium currents in human atrium
AUTHOR(S):	Bosch, R. F.; Milek, I. V.; Popovic, K.; Mermi, J.; Mewis, C.; Kuhlkamp, V.; Seipel, L.
CORPORATE SOURCE:	Department of Cardiology, University of Tübingen, Tübingen, 72076, Germany
SOURCE:	Journal of Cardiovascular Pharmacology (1999), 33(5), 762-771 CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER:	Lippincott Williams & Wilkins
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Ambasilide (LU 47110) is a new class III **antiarrhythmic** drug with a unique profile of action in mammals; however, the effects on human atrial repolarization are not known. We tested the effects of ambasilide on action potentials and repolarizing potassium currents in single atrial myocytes. Ambasilide delayed all phases of repolarization in a concn.-dependent manner [i.e., 10 μ M prolonged the action potential duration to 90% repolarization at 1 Hz from 217.8 ± 34.1 to 360.6 ± 63.0 ms ($p < 0.05$ vs. control)]. Action-potential prolongation was independent of the applied stimulation frequency over a range of 0.5-2 Hz; the drug therefore did not display reverse use dependence. Ambasilide produced a concn.-dependent block of the inward rectifier potassium current (IK1) and the acetylcholine-activated potassium current (IKACH) with a median effective concn. (EC50) of 6.0 and 2.3 μ M, resp. Ambasilide also led to a concn.-dependent inhibition of the transient outward current (Itol; EC50 = 5.7 μ M) and the sustained potassium outward current (Iso; EC50 = 43.6 μ M). The effect of ambasilide was independent of the step voltage (in the range of +20 to +60 mV) or the applied stimulation frequency (0.5-2 Hz). Inactivation kinetics were not altered. Ambasilide is a new class III **antiarrhythmic** drug with a distinct profile of action. Its frequency-independent prolongation of the human atrial action potential makes this group of compds. a promising alternative to currently available class III **antiarrhythmic** drugs.

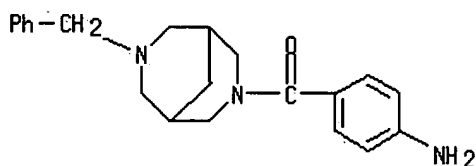
IT 83991-25-7, Ambasilide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**antiarrhythmic** ambasilide prolongs action potential and blocks multiple potassium currents in human atrium)

RN 83991-25-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
(CA INDEX NAME)

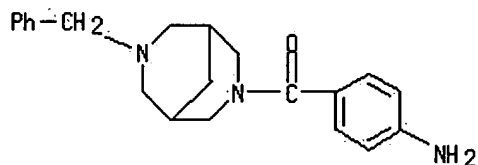


REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1998:90424 HCAPLUS
DOCUMENT NUMBER: 128:225930
TITLE: Rate-independent effects of the new class III **antiarrhythmic** agent ambasilide on transmembrane action potentials in human ventricular endomyocardium
AUTHOR(S): Weyerbrock, Sonja; Schrejeck, Jurgen; Karch, Martin; Overbeck, Matthias; Meisner, Hans; Kemkes, Bernhard; Schomig, Albert; Schmitt, Claus
CORPORATE SOURCE: Klinik fur Herz- und Kreislaferkrankungen, Medizinische Klinik der Technischen Universitat Munchen, Munchen, Germany
SOURCE: Journal of Cardiovascular Pharmacology (1997), 30(5), 571-575
CODEN: JPCPDT; ISSN: 0160-2446
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The electrophysiol. effects of ambasilide, a new class III **antiarrhythmic** drug reported to be a nonselective blocker of both components (IKr and IKs) of the delayed-rectifier potassium current (IK) and other repolarizing potassium currents (ItoI, Iso), were studied in specimens of left ventricular endomyocardium of human hearts obtained from 10 patients undergoing either hear transplantation (n=4) or mitral valve replacement (n=6). We recorded transmembrane action potential (TAP) characteristics at different stimulation frequencies (0.5, 1, 1.5, and 2 Hz) and with different dosages of ambasilide (1, 10, and 50 μ M) by using conventional microelectrode techniques. Beginning at a concn. of 10 μ M ambasilide, the TAP duration at 90% repolarization (TAPD90) was significantly prolonged and independent of stimulation frequency with a mean percentage prolongation of 18% at 10 μ M and 30% at 50 μ M ambasilide. TAP duration at 50% repolarization was not significantly prolonged except for 10 μ M ambasilide at 0.5 Hz (17%; p<0.05). The frequency-independent action potential (AP) prolongation by ambasilide in human ventricular endomyocardium indicates that a nonselective block of repolarizing potassium currents seems to be more favorable than a selective block of IKr.
IT **83991-25-7**, Ambasilide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(rate-independent effects of the new class III **antiarrhythmic** agent ambasilide on transmembrane action potentials in human ventricular endomyocardium)
RN **83991-25-7** HCAPLUS
CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
(CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1997:568227 HCAPLUS
 DOCUMENT NUMBER: 127:229430
 TITLE: Bisaramil and **antiarrhythmics** as inhibitors of free radical generation
 AUTHOR(S): Paroczai, Margit; Roth, Elizabeth; Karpati, Egon
 CORPORATE SOURCE: Pharmacological Research Institute, Chemical Works of Gedeon Richter Ltd, Budapest, H-1475, Hung.
 SOURCE: Pharmacological Research (1997), 35(4), 279-285
 CODEN: PHMREP; ISSN: 1043-6618
 PUBLISHER: Academic
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The aim of this study was to investigate the effect of bisaramil, an **antiarrhythmic** drug under clin. trials, on free radical generation of isolated polymorphic neutrophil granulocytes (PMN) and furthermore to compare its activity to that of well-known **antiarrhythmics** which have different modes of action. PMNs were isolated from healthy beagle dogs, and superoxide radical generation was induced by phorbol-myristate-acetate. Stimulated free radical generation capacity of PMNs and the time lag necessary for the initiation of free radical prodn. were measured. All compds. were used at the concns. of 10, 25, 50, 75, 100 µg ml⁻¹. None of the **antiarrhythmics** stimulated by itself the free radical generation. Bisaramil exerted concn. dependent inhibitory effect on PMA-stimulated free radical generation and prolonged the time lag concn. dependently. At the investigated concn. range of **antiarrhythmics** only propafenon, mexiletine and diltiazem showed similar activity to bisaramil, but clear concn. dependency could not be seen in any of the cases. According to the results of this study inhibition of the stimulated free radical prodn. of isolated PMNs cannot be closely connected merely to either membrane stabilizing or Ca antagonistic activity of drugs. In vitro and earlier measured in vivo inhibitory action of bisaramil on free radical generation indicate a possible cardioprotective effect existing independently from its **antiarrhythmic** one. This observation may be important in outlining of the clin. indication field of bisaramil, and may be useful in the treatment of reperfusional damage.

IT 89194-77-4, Bisaramil

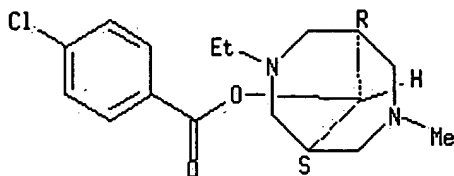
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(bisaramil inhibition of free radical generation: comparison with other **antiarrhythmics** and implications for cardioprotective effect)

RN 89194-77-4 HCAPLUS

CN Benzoic acid, 4-chloro-, (9-syn)-3-ethyl-7-methyl-3,7-diazabicyclo[3.3.1]non-9-yl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



L5 ANSWER 23 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1997:270872 HCAPLUS
 DOCUMENT NUMBER: 127:576
 TITLE: Class III electrophysiologic actions of imidazole-substituted diheterabicyclononanes in canine myocardium
 AUTHOR(S): Patterson, Eugene; Scherlag, Benjamin J.; Sangiah, Subiah; Garrison, Gregory L.; Couch, Kevin M.; Berlin, K. Darrell; Lazzara, Ralph
 CORPORATE SOURCE: Coll. Med., Univ. Oklahoma Health Sci. Cent., Oklahoma City, OK, 73104, USA
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1997), 281(1), 155-162
 CODEN: JPETAB; ISSN: 0022-3565
 PUBLISHER: Williams & Wilkins
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The electrophysiol. effects of the imidazole-substituted diheterabicyclo[3.3.1]nonane compds. GLG-v-13 and KMC-IV-84 were evaluated in canine ventricular tissues using intracellular and extracellular recordings. The drugs produced a concn.-dependent prolongation of action potential duration at 90% of repolarization in Purkinje (338 to 611 ms, 10 mg/L GLG-V-13; 328 to 468 ms, 10 mg/L KMC-IV-84), in right ventricular subendocardium (260 to 335 ms, 10 mg/L GLG-V-13; 221 to 264 ms, 10 mg/L KMC-IV-84) and in left ventricular epicardium (195 to 256 ms, 10 mg/L GLG-V-13; 203 to 273 ms, 10 mg/L KMC-IV-84) without altering resting membrane potential, action potential amplitude, overshoot potential, Vmax, conduction velocity or Purkinje fiber automaticity. Prolongation of the effective refractory period was proportional to the change in action potential duration at 90% of repolarization. Prolongation of action potential duration at 90% of repolarization was maximal at paced cycle lengths exceeding 1000 ms and was minimal at a paced cycle length of 250 ms (Purkinje: 266 vs. 6 ms, GLG-V-13; 178 vs. 10 ms, KMC-IV-84; right ventricular subendocardium: 70 vs. 10 ms, GLG-V-13; 60 vs. 19 ms.; left ventricular epicardium: 67 vs. 10 ms, GLG-V-13; 68 vs. 16 ms, KMC-IV-84). An increase in K⁺o to 12 mM reduced action potential prolongation by GLG-V-13 and KMC-IV-84 in left ventricular epicardium. The results demonstrate selective class III **antiarrhythmic** electrophysiol. properties for imidazole-substituted diheterabicyclo[3.3.1]nonane compds.

IT 155029-33-7, GLG-v-13

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

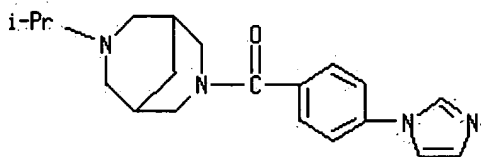
(class III **antiarrhythmic** electrophysiol. actions of imidazole-substituted diheterabicyclononanes in canine myocardium)

RN 155029-33-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-[4-(1H-imidazol-1-yl)benzoyl]-7-(1-methylethyl)-, diperchlorate (9CI) (CA INDEX NAME)

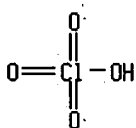
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CM 2

CRN 7601-90-3
CMF C1 H O4



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 24 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:	1997:50418 HCAPLUS
DOCUMENT NUMBER:	126:84362
TITLE:	Effects of bisarrhythmic on coronary-occlusion-reperfusion injury and free-radical-induced reactions
AUTHOR(S):	Paroczai, Margit; Roth, Elizabeth; Matos, Gabor; Temes, Gyula; Lantos, Janos; Karpati, Egon
CORPORATE SOURCE:	Pharmacological Research Centre, Chemical Works of Gedeon, Budapest, H-1475, Hung.
SOURCE:	Pharmacological Research (1996), 33(6), 327-336 CODEN: PHMREP; ISSN: 1043-6618
PUBLISHER:	Academic
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The aim of this study was to det. whether bisarrhythmic - an **antiarrhythmic** compd. under clin. investigation - influences the reperfusion-induced **arrhythmic** and biochem. parameters characterizing occlusion-reperfusion-induced free-radical reactions. The left descending coronary artery (LAD) was occluded for 60 min in anesthetized dogs followed by one hour of reperfusion. Blood samples were taken at different times of the occlusion and reperfusion for the detn. of plasma concn. of malondialdehyde (MDA), reduced (GSH) and oxidized glutathione (GSSG); furthermore of the activity of catalase and superoxide dismutase (SOD). Free-radical generating capacity of polymorph neutrophil granulocytes (PMN) was also measured. At the end of the expts. heart tissue samples were excised from the injured areas and from the intact part of the left ventricular muscle. In tissue samples the concns. of MDA and GSH and the activity of SOD were detd. Bisarrhythmic was given as an i.v. bolus injection at a dose of 2 mg kg⁻¹ several minutes prior to the end of LAD-occlusion; then the administration was repeated in the 30th minute of reperfusion. In the control group (10 dogs) ventricular fibrillation (VF) occurred in seven cases which resulted in death in three. In the bisarrhythmic-treated group, however, VF was seen

in three cases and no death was recorded. Bisaramil inhibited the elevation of the plasma concn. of MDA and GSSG during the reperfusion and abolished the decrease in the plasma concn. of GSH during the occlusion and reperfusion. The activity of SOD and catalase in plasma was much better preserved in the bisaramil-treated group than in the controls. Bisaramil significantly inhibited the increase of the superoxide-radical generating capacity of PMNs during the reperfusion. The data obtained from myocardial tissue samples supported the cardioprotective effect of bisaramil. The biochem. investigation of ischemic-reperfused myocardium showed that bisaramil promoted preservation of SOD-activity and of tissue glutathione. Results of this study clearly showed that bisaramil has a significant effect on ischemia-reperfusion induced **arrhythmias**; it has a special benefit in influencing free-radical mediated damage leading to better preservation of membranes and to limitations of irreversible cell injuries.

IT 89194-77-4, Bisaramil

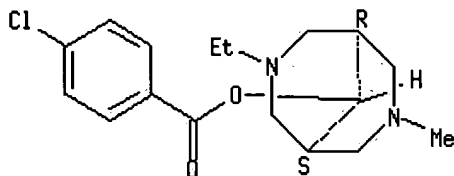
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(effects of bisaramil on coronary-occlusion-reperfusion injury and free-radical-induced reactions)

RN 89194-77-4 HCAPLUS

CN Benzoic acid, 4-chloro-, (9-syn)-3-ethyl-7-methyl-3,7-diazabicyclo[3.3.1]non-9-yl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



L5 ANSWER 25 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1996:495746 HCAPLUS

DOCUMENT NUMBER: 125:316687

TITLE: Differential class III **antiarrhythmic** effects of ambasilide and dofetilide at different extracellular potassium and pacing frequencies

AUTHOR(S): Gjini, Viktor; Korth, Michael; Schreieck, Juergen; Weyerbrock, Sonja; Schoemig, Albert; Schmitt, Claus

CORPORATE SOURCE: Med. Klinik, Tech. Univ., Munich, Germany

SOURCE: Journal of Cardiovascular Pharmacology (1996), 28(2), 314-320

CODEN: JCPCDT; ISSN: 0160-2446

PUBLISHER: Lippincott-Raven

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We studied the effect of two new class III **antiarrhythmics**, ambasilide and dofetilide, on the action potential duration (APD) of guinea pig right ventricular papillary muscle at different extracellular potassium concns. ([K⁺e]) and pacing frequencies. Under normal [K⁺e], both drugs significantly prolonged APD₉₀ (APD at 90% repolarization) at 0.5 Hz. The effect of ambasilide was well preserved at rapid pacing rates, independent of [K⁺e]. The effect of dofetilide was markedly reduced with increasing pacing rate, esp. in high [K⁺e]. Therefore, ambasilide may be useful in

treating **tachyarrhythmias** in normal, as well as in altered [K⁺e] conditions.

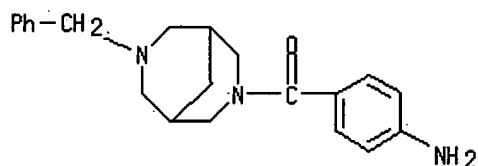
IT **83991-25-7**, Ambasilide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(differential class III **antiarrhythmic** effects of ambasilide and dofetilide at different extracellular potassium and pacing frequencies)

RN **83991-25-7** HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
(CA INDEX NAME)



L5 ANSWER 26 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1996:495729 HCAPLUS

DOCUMENT NUMBER: 125:316677

TITLE: Electrophysiological and inotropic characterization of a novel class III **antiarrhythmic** agent, GLG-V-13, in the mammalian heart

AUTHOR(S): Fazekas, Tamas; Carlsson, Leif; Scherlag, Benjamin J.; Mabo, Philippe; Poty, Herve; Palmer, Mattias; Patterson, Eugene; Berlin, K. Darrell; Garrison, Gregory L.; Lazzara, Ralph

CORPORATE SOURCE: 1st Dep. Med., Szent-Gyorgyi Univ. Med. Sch., Szeged, Hung.

SOURCE: Journal of Cardiovascular Pharmacology (1996), 28(2), 182-191

CODEN: JCPCDT; ISSN: 0160-2446

PUBLISHER: Lippincott-Raven

DOCUMENT TYPE: Journal

LANGUAGE: English

AB GLG-V-13, a novel 3,7-diheterabicyclo(3.3.1)nonane, was examd. both in vivo and in vitro to characterize its electrophysiol., hemodynamic, and inotropic properties. In anesthetized guinea pigs, GLG-V-13 [0.5-500 µg/kg i.v.] lengthened the epicardial monophasic action potential (MAP) duration, the atrioventricular (AV) conduction time and the RR interval in a dose-dependent manner. At the highest dose, these variables were increased by 30, 13, and 23%, resp. No significant effects were noted on QRS duration or blood pressure (BP). In rabbit atrial and papillary muscle preps., GLG-V-13 (0.32-3.2 mg/L) did not exert a neg. inotropic action and in isolated rabbit cardiomyocytes the agent blocked the rapidly activating delayed rectifier K⁺ current (IKr, EC50 = 48 µg/L). In 10 intact anesthetized mongrel dogs, the left ventricular (LV) endocardial MAP was measured during atrial pacing before and after administration of GLG-V-13 (3 and 6 mg/kg i.v.). As compared with the drug-free state, the agent induced a significant prolongation of the MAP at all pacing frequencies (2.0-4.5 Hz). In 15 anesthetized dogs studied 1-4 days after two-stage ligation of the left anterior descending coronary artery (LAD), the **antiarrhythmic/proarrhythmic** potential of GLG-V-13 was compared with that of lidocaine. ECG, His bundle, LV (IZepi), and composite and

normal zone composite electrograms were recorded. Programmed elec. stimulation (PES) and burst pacing (4.0-7.0 Hz) were delivered to the right ventricular outflow tract. In the drug-free state, sustained monomorphic ventricular tachycardia (SMVT) was inducible in 6 dogs (6 of 15). After lidocaine, SMVT was induced in 7 other dogs (13 of 15). GLG-V-13 prevented induction of SMVT in 5 of 6 dogs; a **proarrhythmic** action was noted in 1 dog only. GLG-V-13 slowed the heart rate (HR), increased the AH and the HV intervals, prolonged the paced (2.5 Hz) QT interval, and increased the ventricular effective refractory period (VERP). These effects were assocd. with 2:1 block of late potentials in the IZepi electrograms, a phenomenon also obsd. during rapid atrial pacing (2.5-3.5 Hz), suggestive of a marked prolongation of refractoriness in the ischemia-damaged myocardium. In light of the recent Cardiac Arrhythmia Suppression Trial (CAST) study, the **antiarrhythmic** efficacy, together with the low **proarrhythmic** potential and lack of cardiodepressant properties of GLG-V-13, may merit further investigation of this novel class III **antiarrhythmic** agent.

IT 155029-33-7, GLG-V-13

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(electrophysiol. and inotropic characterization of a novel class III **antiarrhythmic** agent, GLG-V-13, in the mammalian heart)

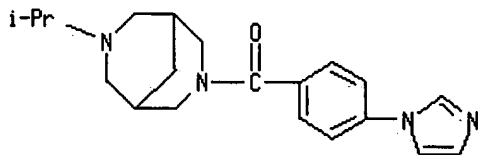
RN 155029-33-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-[4-(1H-imidazol-1-yl)benzoyl]-7-(1-methylethyl)-, diperchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 155029-32-6

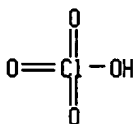
CMF C20 H26 N4 O



CM 2

CRN 7601-90-3

CMF Cl H O4



L5 ANSWER 27 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing
References

ACCESSION NUMBER: 1996:105098 HCAPLUS

DOCUMENT NUMBER: 124:193859

TITLE: Effects of the class III **antiarrhythmic** drug ambasilide on outward currents in human atrial myocytes

AUTHOR(S): Koidl, Bernd; Flaschberger, Peter; Schaffer, Peter; Pelzmann, Brigitte; Bernhart, Eva; Maechler, Heinrich; Rigler, Bruno

CORPORATE SOURCE: Institut Medizinische Physik Biophysik, Universitaet Graz, Graz, A-8010, Austria

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1996), 353(2), 226-32
CODEN: NSAPCC; ISSN: 0028-1298

PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

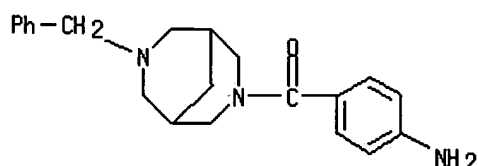
AB We have studied the inhibitory influence of the class III **antiarrhythmic** drug ambasilide (LU 47110) on the transient outward current I_{to1} and the sustained current I_{so} following inactivation of I_{to1} , in human atrial myocytes. The two currents are sep'd. by a math. procedure based on the amplitudes and time consts. of the biexponential inactivation of the total outward current. The frequency dependence, the recovery from inactivation and the kinetics of activation and inactivation are described. Ambasilide reversibly and concn. dependently inhibited I_{to1} , I_{so} and the sodium current I_{Na} . Concn. required for half maximal inhibition (IC_{50}) for the effects on I_{to1} and I_{so} were $23.3 \mu\text{mol/l}$ and $45.7 \mu\text{mol/l}$ resp., concns. shown by others to be effective in terminating and preventing fibrillation in a dog atrial **arrhythmia** model. Ambasilide not only reduced the amplitude of I_{to1} and I_{so} but also accelerated the time course of inactivation from 14.22 to 6.69 ms and from 202.3 to 87.9 ms resp. The amplitude of I_{to1} showed only a small dependence on stimulation frequency characteristic for human atrial myocytes, whereas I_{so} was reduced significantly at higher stimulation frequencies. Ambasilide did not change these relationships (0.1-4 Hz) and therefore did not show the reverse use-dependence known from other class III **antiarrhythmic** agents and which is an important property for a prospective **antiarrhythmic** drug. The lack of an effect of ambasilide on both steady-state activation and inactivation of I_{to1} , and the time const. of recovery from inactivation, suggests that ambasilide acts by changing conductance rather than by influencing the gating mechanism. The described characteristics make ambasilide an interesting substance in the group of class III **antiarrhythmic** drugs.

IT 83991-25-7, Ambasilide

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(class III **antiarrhythmic** drug ambasilide effect on outward currents in human atrial myocytes)

RN 83991-25-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
(CA INDEX NAME)



L5 ANSWER 28 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1995:1006741 HCAPLUS

DOCUMENT NUMBER: 124:176165

TITLE: N-alkyl and N-acyl derivatives of 3,7-diazabicyclo[3.3.1]nonanes and selected salts thereof

as multi-class **antiarrhythmic** agents

INVENTOR(S): Berlin, Kenneth D.; Garrison, Gregory L.; Sangiah, Subbiah; Clarke, Cyril R.; Chen, Chun Lin; Lazzara, Ralph; Scherlag, Benjamin J.; Patterson, Eugene S.; Burrows, George E.

PATENT ASSIGNEE(S): Oklahoma State University, USA

SOURCE: U.S., 20 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

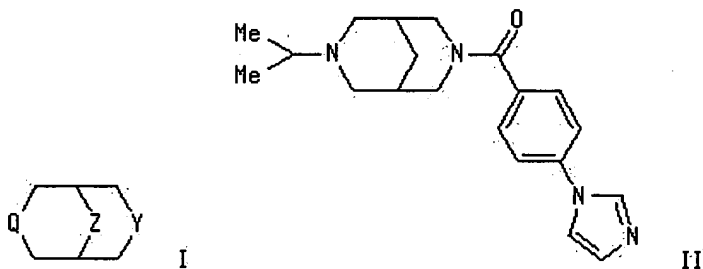
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5468858	A	19951121	US 1993-144639	19931028
US 5786481	A	19980728	US 1995-545341	19951019
PRIORITY APPLN. INFO.:			US 1993-144639	19931028
OTHER SOURCE(S):	MARPAT 124:176165			

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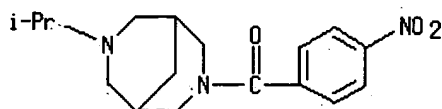
AB A variety of 3,7-diazabicyclo[3.3.1]nonanes and selected derivs. are disclosed as multi-class **antiarrhythmic** agents and intermediates thereof. Claimed compds. include I [Q = RN where R = iso-Pr or cyclopropylmethyl; Z = CH₂; Y = ArCON where Ar = (un)substituted aryl] and their hydrochloride, hydroperchlorate, fumarate, and other salts. For example, 3-isopropyl-3,7-diazabicyclo[3.3.1]nonane underwent N-acylation with 4-FC₆H₄COCl, and the product fluoride was condensed with imidazole in the presence of K₂CO₃ and 18-crown-6, to give title compd. II, isolated as the dihydroperchlorate. At 3-6 mg/kg in dogs with myocardial infarctions and induced ventricular tachycardia, II increased ventricular effective refractory period, prolonged QT by 30%, lowered heart rate by 20-40 beats/min, and prevented sustained ventricular tachycardia (Class I and III activity).

IT **173973-20-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**;
THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (prepn. of N-alkyl and N-acyl diazabicyclononane derivs. as multi-class **antiarrhythmics**)

RN **173973-20-1** HCAPLUS

CN **3,7-Diazabicyclo[3.3.1]nonane, 3-(1-methylethyl)-7-(4-nitrobenzoyl)-** (9CI)
 (CA INDEX NAME)



L5 ANSWER 29 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1995:915127 HCAPLUS
 DOCUMENT NUMBER: 123:305992
 TITLE: Comparative Evaluation of the Predictive Power of Calculation Procedures for Molecular Lipophilicity
 AUTHOR(S): Mannhold, Raimund; Rekker, Roelof F.; Sonntag, Christoph; Ter Laak, Anton M.; Dross, Karl; Polymeropoulos, Emmanuel E.
 CORPORATE SOURCE: Department of Lasermedicine, Heinrich-Heine-Universitaet, Duesseldorf, 40225, Germany
 SOURCE: Journal of Pharmaceutical Sciences (1995), 84(12), 1410-19
 CODEN: JPMSAE; ISSN: 0022-3549
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The predictive power of four calcn. procedures for mol. lipophilicity is checked by comparing with exptl. data (log P and chromatog. RMw) taken from the literature. Two sets of test compds. are used: the first comprises simple org. mols. and the second consists of more complicated drug mols. Our comparative evaluation leads us to conclude that the predictive power is significantly better for not too complicated org. mols. than for drugs with complicated structural pattern. The four investigated calcn. procedures should be arranged in two groups with significantly differing predictive power: (a) Rekker and Hansch/Leo and (b) Ghose/Crippen and Suzuki/Kudo. This conclusion is based on a statistical control using log P and RMw as the independent parameters. Correlations have in common: (1) slopes in correlations with calcd. data based on fragmental methods are not significantly different from 1; calcns. with data from atom-based procedures show up in most cases with slopes below 1. (2) The accompanying overall statistics underline the superiority of the fragmental methods. We think that all four tested calcn. procedures have their own restrictions; for future development we would advise a thorough reconsideration of structural effects not fully (or even not at all) incorporated in the data sets. Special attention will have to be paid to the conformational aspects of lipophilic behavior:

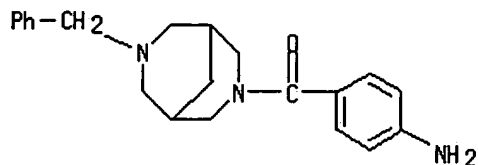
IT 83991-25-7, Ambasilide

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(comparative evaluation of the predictive power of calcn. procedures for mol. lipophilicity)

RN 83991-25-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
 (CA INDEX NAME)



L5 ANSWER 30 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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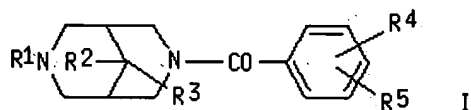
ACCESSION NUMBER: 1995:785013 HCAPLUS
DOCUMENT NUMBER: 123:188602
TITLE: **Antiarrhythmic** 3-benzoyl-3,7-diazabicyclo[3.3.1]nonanes
INVENTOR(S): Schoen, Uwe; Brueckner, Reinhard; Meil, Joerg; Thormaehlen, Dirk
PATENT ASSIGNEE(S): Kali-Chemie Pharma GmbH, Germany
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 665014	A1	19950802	EP 1995-100953	19950125
EP 665014	B1	19970903		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
DE 4402933	A1	19950803	DE 1994-4402933	19940201
IL 112344	A1	19970610	IL 1995-112344	19950116
CN 1110556	A	19951025	CN 1995-101603	19950125
AT 157539	E	19970915	AT 1995-100953	19950125
ES 2108497	T3	19971216	ES 1995-100953	19950125
HU 70173	A2	19950928	HU 1995-263	19950127
CA 2141367	AA	19950802	CA 1995-2141367	19950130
AU 9511468	A1	19950810	AU 1995-11468	19950130
ZA 9500698	A	19960207	ZA 1995-698	19950130
PL 184904	B1	20030131	PL 1995-307001	19950130
FI 9500423	A	19950802	FI 1995-423	19950131
NO 9500361	A	19950802	NO 1995-361	19950131
JP 07252152	A2	19951003	JP 1995-14209	19950131
US 5532251	A	19960702	US 1995-382265	19950201

PRIORITY APPLN. INFO.: DE 1994-4402933 A 19940201

OTHER SOURCE(S): MARPAT 123:188602

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AB The title compds. (I; R1 = C1-6 alkyl, C4-7 cycloalkylalkyl; R2, R3 = lower alkyl, or R2R3 = C3-6 alkylene; R5 = H, halo, CF3, NO2; R4 = R5, CN, R6SO2; R6 = F, lower alkyl) and their acid addn. salts are useful for treatment of **arrhythmia** in humans and large mammals. Thus, I [R1 = Bu, R2R3 = (CH2)4, R4 = 4-chloro, R5 = H] (II) (2 μ mol/kg i.v.) prolonged the effective refractory time in guinea pigs with exptl. tachycardia by 15% and had a min. oral toxic dose of >300 mg/kg in mice. Tablets were prepd. contg. II-HCl 20, corn starch 30, lactose 55, PVP-25 5, Mg stearate 2, and talc 3 parts. II was prepd. by condensation of 7-butyl-9,9-tetramethylene-3,7-diazabicyclo[3.3.1]nonane with 4-chlorobenzoyl chloride.

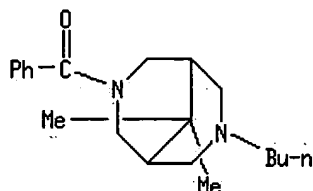
IT **167553-54-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiarrhythmic benzoyldiazabicyclononanes)

RN 167553-54-0 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-benzoyl-7-butyl-9,9-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)



HCl

L5 ANSWER 31 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1995:785009 HCAPLUS

DOCUMENT NUMBER: 123:188601

TITLE: Antiarrhythmic 3-phenylsulfonyl-3,7-diazabicyclo[3.3.1]nonanes

INVENTOR(S): Schoen, Uwe; Farjam, Arman; Brueckner, Reinhard; Ziegler, Dieter

PATENT ASSIGNEE(S): Kali-Chemie Pharma GmbH, Germany

SOURCE: Eur. Pat. Appl., 20 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

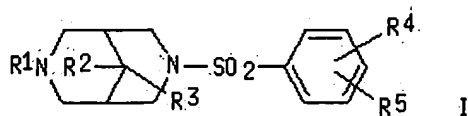
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 665228	A1	19950802	EP 1995-100954	19950125
EP 665228	B1	19990714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
DE 4402931	A1	19950803	DE 1994-4402931	19940201
IL 112364	A1	19980104	IL 1995-112364	19950117
CN 1111631	A	19951115	CN 1995-101498	19950125
AT 182149	E	19990715	AT 1995-100954	19950125
ES 2133593	T3	19990916	ES 1995-100954	19950125
HU 70174	A2	19950928	HU 1995-262	19950127
CA 2141366	AA	19950802	CA 1995-2141366	19950130
AU 9511564	A1	19950810	AU 1995-11564	19950130
ZA 9500697	A	19960207	ZA 1995-697	19950130
PL 180075	B1	20001229	PL 1995-307000	19950130
FI 9500422	A	19950802	FI 1995-422	19950131
NO 9500360	A	19950802	NO 1995-360	19950131
JP 07267954	A2	19951017	JP 1995-14204	19950131
US 5576327	A	19961119	US 1995-382262	19950201
US 5635511	A	19970603	US 1996-594946	19960131

PRIORITY APPLN. INFO.: DE 1994-4402931 A 19940201
US 1995-382262 A3 19950201

OTHER SOURCE(S): MARPAT 123:188601

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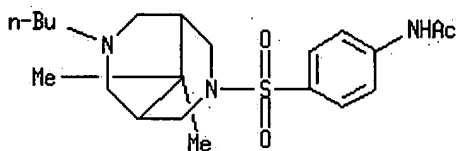
AB The title compds. (I; R1 = C1-6 alkyl, C4-7 cycloalkylalkyl; R2, R3 = lower alkyl, or R2R3 = C3-6 alkylene; R4 = halo, NO₂, CF₃, CN, alkoxy carbonyl, alkanesulfonamido, carboxamido; R5 = H, halo) are useful for treatment of cardiac **arrhythmia** in humans and large mammals. Thus, I (R1 = Bu, R2 = R3 = Me, R4 = 4-CN, R5 = H) (II) (1 μmol/kg i.v.) prolonged the effective refractory time by 15% in guinea pigs with exptl. tachycardia, and had a min. oral toxic dose >300 mg/kg in mice. II-HCl was prepd. by condensation of 7-butyl-9,9-dimethyl-3,7-diazabicyclo[3.3.1]nonane with 4-cyanobenzenesulfonyl chloride. Tablets were prepd. contg. II-HCl 20, corn starch 69, lactose 135, gelatin (as 10% soln.) 6, talc 5, and Mg stearate 5 mg.

IT 167552-72-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (antiarrhythmic phenylsulfonyldiazabicyclononanes)

RN 167552-72-9 HCAPLUS

CN Acetamide, N-[4-[(7-butyl-9,9-dimethyl-3,7-diazabicyclo[3.3.1]non-3-yl)sulfonyl]phenyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 32 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:	1995:646211 HCAPLUS
DOCUMENT NUMBER:	123:74487
TITLE:	Electrophysiological characterization of a novel class III antiarrhythmic agent, GLG-V-13 in the mammalian heart
AUTHOR(S):	Fazekas, T.; Scherlag, B. J.; Carlsson, L.; Mabo, P.; Patterson, E.; Berlin, K. D.; Lazzara, R.
CORPORATE SOURCE:	Health Sciences Center, University of Oklahoma, Oklahoma City, OK, H-6701, USA
SOURCE:	Acta Physiologica Hungarica (1995), 83(1), 13-30 CODEN: APHHDU; ISSN: 0231-424X
PUBLISHER:	Akademiai Kiado
DOCUMENT TYPE:	Journal
LANGUAGE:	English
AB	GLG-V-13, a novel 3,7-diheterabicyclo[3.3.1]nonane, was examd. both in vivo and in vitro in order to characterize its electrophysiol., hemodynamic and inotropic properties. Left ventricular epicardial monophasic action potential (MAP), surface ECG and mean arterial blood pressure (MBP) were recorded in six pentobarbital-anesthetized,

artificially ventilated and thoracotomized guinea-pigs. When studied in an i.v. dose interval ranging between 0.5 µg/kg and 500 µg/kg, GLG-V-13 dose-dependently lengthened the MAP duration ($p < 0.05$ at doses above 5 µg/kg), the atrioventricular conduction time ($p < 0.05$ at doses above 1 µg/kg) and the RR interval ($p < 0.05$ at doses above 25 µg/kg). At the highest dose (500 µg/kg) these variables were increased by 30%, 13% and 23%, resp. Only minor effects were noted on intraventricular conduction time (QRS interval) and MBP. In rabbit atrial and papillary muscle preps., GLG-V-13 (0.32 to 3.2 mg/L) did not exert neg. inotropic action. In 10 intact anesthetized mongrel dogs, left ventricular endocardial MAP at 90% repolarization (MAP90) was measured during atrial pacing before and after administration of GLG-V-13, 3 and 6 mg/kg i.v., resp.

IT 155029-33-7, GLG-V-13

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(electrophysiol. characterization of novel class III antiarrhythmic agent, GLG-V-13 in heart)

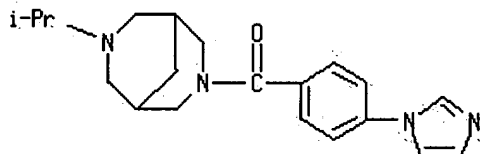
RN 155029-33-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-[4-(1H-imidazol-1-yl)benzoyl]-7-(1-methylethyl)-, diperchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 155029-32-6

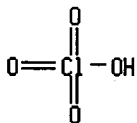
CMF C20 H26 N4 O



CM 2

CRN 7601-90-3

CMF Cl H O4



L5 ANSWER 33 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1995:644358 HCAPLUS

DOCUMENT NUMBER: 123:74508

TITLE: Effects on atrial repolarization of the interaction between K⁺ channel blockers and muscarinic receptor stimulation

AUTHOR(S): Zaza, Antonio; Malfatto, Gabriella; Schwartz, Peter J.

CORPORATE SOURCE: Dep. Fisiologia Biochimica Generali, Univ. Milan, Milan, Italy

SOURCE: Journal of Pharmacology and Experimental Therapeutics

(1995), 273(3), 1095-104

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER:

Williams & Wilkins

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The authors have tested, in guinea pig atria, how muscarinic stimulation by oxotremorine (Oxo) modifies the effects on action potential duration (APD) of two iK blockers: d-sotalol (5 μ M) and ambasilide (1 μ M). APD was prolonged by d-sotalol (+34.8%) and ambasilide (+54.2%). Simultaneous superfusion with Oxo 0.5 μ M markedly shortened APD; this effect was larger in the presence of d-sotalol than in the presence of ambasilide (-69% vs. -37.4%). Moreover ambasilide, but not d-sotalol, antagonized APD shortening induced by Oxo. The basis for such a difference between the two drugs was studied in patch-clamp expts. on isolated rabbit atrial and sinoatrial myocytes. Besides blocking iK (half-effective concn.: EC50 = 2 μ M), ambasilide almost completely inhibited iKACH (-86% at 10 μ M; EC50 = 1.6 μ M), which was minimally affected by d-sotalol. Ambasilide 2 μ M increased 10-fold the acetylcholine (ACh) required for 50% iKACH activation, and reduced maximally activated iKACH by 18.8%. When iKACH was activated through a receptor-independent mechanism, 10 μ M ambasilide reduced this current by only 18.7% of its control value. Moreover, ambasilide, although not affecting the current if in basal conditions, reversed its inhibition by ACh. Thus, (1) the effect of K⁺ channel blockers on atrial APD may be blunted by ACh; ambasilide effects are less sensitive to ACh than those of d-sotalol; (2) ambasilide, but not d-sotalol, inhibits iKACH, this probably occurs largely, although not exclusively, through muscarinic receptor antagonism. Inhibition of iKACH may account for the persistence of the effects of this drug on atrial APD despite muscarinic stimulation. The results are discussed in relation to the atrial **antiarrhythmic** actions of potassium channel blockers.

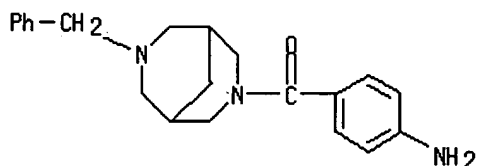
IT 83991-25-7, Ambasilide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effects on atrial repolarization of the interaction between K⁺ channel blockers and muscarinic receptor stimulation in relation to **antiarrhythmic** activity)

RN 83991-25-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
(CA INDEX NAME)



L5 ANSWER 34 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:

1995:589887 HCAPLUS

DOCUMENT NUMBER:

123:218110

TITLE:

Antiarrhythmic effects of bisaramil on triggered **arrhythmias** produced by intracoronary injection of digitalis and adrenaline in the dog

AUTHOR(S):

Haruno, Akihiro; Hashimoto, Keitaro

CORPORATE SOURCE: Dep. Pharmacol., Yamanashi Med. Univ., Yamanashi,
409-38, Japan
SOURCE: Japanese Journal of Pharmacology (1995), 68(1), 95-102
CODEN: JJPAAZ; ISSN: 0021-5198
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Antiarrhythmic** effects of bisaramil were examd. by using new in vivo triggered **arrhythmia** models, and they were compared with those of other **antiarrhythmic** drugs. Bisaramil (3-10 μ g, i.c.) suppressed triggered ventricular **arrhythmias** that were produced during pauses between trains of rapid ventricular stimulation (cycle length: 250 ms, train no.: 15) in anesthetized open-chest dogs administered with subtoxic doses of digitalis or adrenaline to the anterior descending coronary artery. The potencies of bisaramil, disopyramide, lidocaine and flecainide suppressing digitalis-induced triggered ventricular **arrhythmias** were similar to those suppressing adrenaline-induced ones. The potency of verapamil for suppressing digitalis-induced triggered ventricular **arrhythmias** were weaker than that for suppressing the adrenaline-induced ones. Bisaramil was the most effective among the **antiarrhythmic** drugs used in the present expt. Since bisaramil has been reported to be effective in suppressing other canine automatic ventricular **arrhythmias**, and the triggered ventricular **arrhythmias** occur in clin. situations, bisaramil may become a useful drug for the treatment of clin. **arrhythmias**.

IT **89194-77-4**, Bisaramil

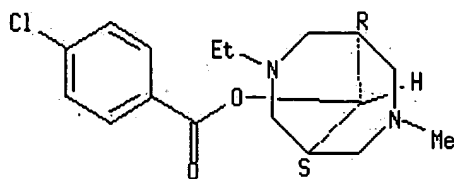
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**antiarrhythmic** effects of bisaramil on triggered **arrhythmias** produced by intracoronary injection of digitalis and adrenaline in the dog)

RN **89194-77-4** HCAPLUS

CN Benzoic acid, 4-chloro-, (9-syn)-3-ethyl-7-methyl-3,7-diazabicyclo[3.3.1]non-9-yl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



L5 ANSWER 35 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1995:533887 HCAPLUS

DOCUMENT NUMBER: 122:281811

TITLE: Effects of the potassium channel blocking agent ambasilide on ventricular **arrhythmias** induced by acute myocardial ischemia and sympathetic activation
AUTHOR(S): Stramba-Badiale, Marco; Pessano, Paolo; Kirchengast, Michael; Schwartz, Peter J.

CORPORATE SOURCE: Istituto di Clinica Medica Generale e Terapia Medica, Universita di Milano, Milan, 20122, Italy

SOURCE: American Heart Journal (1995), 129(3), 549-56
CODEN: AHJOA2; ISSN: 0002-8703

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The ineffectiveness of traditional **antiarrhythmic** agents in preventing sudden cardiac death has increased the interest in drugs that prolong refractoriness. Ambasilide is a new potassium channel blocking agent that appears to prolong refractoriness at short and long cycle lengths. We assessed the effects of ambasilide, 5 mg/kg i.v. (i.v.) bolus plus 5 mg Σ kg⁻¹ Σ h⁻¹ i.v. infusion, in 16 anesthetized cats in which ventricular **arrhythmias** could be induced reproducibly by the combination of acute myocardial ischemia and increased sympathetic activity. Ambasilide decreased heart rate and blood pressure and prolonged QRS duration (26%, $p < 0.05$), QTc (17%, $p < 0.0001$), and JTc (16%, $p < 0.005$). Ambasilide also shifted the strength-interval curve for ventricular refractoriness by 17 to 22 ms to the right ($p < 0.01$). Ventricular fibrillation was obsd. in 7 animals and never occurred after ambasilide ($p < 0.001$); however, 4 (57%) of these cats had sustained ventricular tachycardia requiring cardiac massage. Ambasilide prevented nonsustained ventricular tachycardia in 2 (40%) of 5 animals. The **antiarrhythmic** effect of ambasilide persisted when heart rate was kept const. by atrial pacing. In no case was **proarrhythmia** obsd. Ambasilide had a significant electrophysiol. effect at the ventricular level in the cat because it did prolong QTc and ventricular refractoriness. Therefore ambasilide showed an antifibrillatory effect but provided only a partial protection against lethal **arrhythmias** induced by acute myocardial ischemia and sympathetic activation.

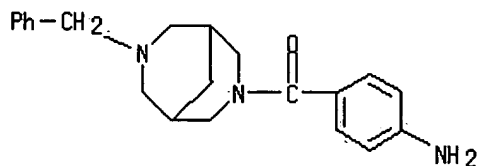
IT **83991-25-7**, Ambasilide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(effects of potassium channel blocking agent ambasilide on ventricular **arrhythmias** induced by acute myocardial ischemia and sympathetic activation)

RN **83991-25-7** HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
(CA INDEX NAME)



L5 ANSWER 36 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1995:329650 HCAPLUS

DOCUMENT NUMBER: 122:96154

TITLE: Tonic and use-dependent block of sodium currents in isolated cardiac myocytes by bisaramil

AUTHOR(S): Pugsley, Michael K.; Saint, David A.

CORPORATE SOURCE: Fac. Med., Univ. British Columbia, Vancouver, BC, V6T 1Z3, Can.

SOURCE: British Journal of Pharmacology (1995), 114(2), 377-82
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Stockton

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of bisaramil on sodium currents in rat isolated cardiac myocytes were examd. by use of tight-seal, whole-cell patch clamp

techniques. Bisaramil produced a concn.-dependent, readily reversible redn. in peak transient sodium current. When the sodium current was evoked at 3 s intervals the estd. ED50 for bisaramil was about 11 μM . Bisaramil (16 μM) produced a shift in the inactivation curve to hyperpolarized potentials of about 10 mV, but produce no change in the voltage-dependence of activation. The block of the sodium current by bisaramil showed a profound use-dependence. A concn. of 10 μM produced a considerable block of the current with repeated stimulation. The recovery from block was biphasic, showing fast and slow components which had time consts. of about 40 ms and 5 s resp. Bisaramil produced little tonic block of the sodium current at concns. of 100 μM ; at 300 μM it produced tonic block of around 50%, with extreme use-dependence. Bisaramil appeared not to interact primarily with the inactivated form of the channel, since lengthening the depolarizing pulses did not affect the degree of block produced.

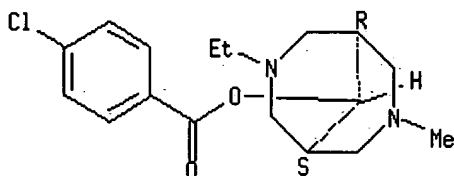
IT **89194-77-4**, Bisaramil

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tonic and use-dependent block of sodium currents in cardiac myocytes by bisaramil)

RN **89194-77-4** HCAPLUS

CN Benzoic acid, 4-chloro-, (9-syn)-3-ethyl-7-methyl-3,7-diazabicyclo[3.3.1]non-9-yl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



L5 ANSWER 37 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1994:692360 HCAPLUS

DOCUMENT NUMBER: 121:292360

TITLE: class III **antiarrhythmic** drug action in experimental atrial fibrillation. Differences in reverse use dependence and effectiveness between d-sotalol and the new **antiarrhythmic** drug ambasilide

AUTHOR(S): Wang, Jinjun; Feng, Jianlin; Nattel, Stanley
CORPORATE SOURCE: Department of Medicine, Montreal Heart Institute, Montreal, H1T 1C8, Can.

SOURCE: Circulation (1994), 90(4), 2032-40
CODEN: CIRCAZ; ISSN: 0009-7322

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Drug therapy to maintain sinus rhythm in patients with atrial fibrillation (AF) is limited by adverse effects and inadequate efficacy. There has been an increased interest in the use of class III drugs to treat AF, and several new agents have been developed, but there is little information available about mechanisms of class III drug action in AF. The present study was designed to compare the effects of two class III agents, d-sotalol and ambasilide, in dog models of exptl. AF. A previously developed dog model of sustained vagotonic AF was used to assess the ability of equal loading doses of d-sotalol and ambasilide (2 mg/kg, followed by maintenance infusions), to terminate AF and prevent its induction. At this dose, ambasilide terminated AF in 12 of 12 dogs and

prevented AF induction in 10 of 12 dogs; d-sotalol terminated AF in 1 of 8 dogs (vs. ambasilide) and prevented AF induction in none of 8 dogs. An addnl. dose of d-sotalol (cumulative load, 8 mg/kg) terminated AF in 7 of 8 dogs and prevented induction in 5 of 8 dogs. In an addnl. 6 dogs with sterile pericarditis and inducible AF, ambasilide prevented AF induction in all 6. An equal dose of d-sotalol (2 mg/kg) failed to suppress AF induction in any dog, but 8 mg/kg of d-sotalol suppressed AF induction in all. Atrial effective refractory period (AERP) was increased by both drugs. However, the effects of d-sotalol on AERP showed strong reverse use dependence, whereas those of ambasilide did not. Neither ambasilide nor d-sotalol significantly altered conduction velocity, and both increased ventricular refractoriness, with d-sotalol once again showing more reverse use dependence. EDs of both agents increased AERP and the wavelength for atrial reentry at rapid rates, slowing atrial activation and terminating the **arrhythmia**. The class III drugs d-sotalol and ambasilide terminate AF by increasing AERP and the wavelength for reentry. Ambasilide, which has been reported to block both the rapid and slow components of the delayed rectifier (IKr and IKs), shows less reverse use dependence of effects on refractoriness than the pure IKr blocker d-sotalol, possibly explaining the greater effectiveness of ambasilide at an equal dose level. These results indicate that class III drugs can exhibit different profiles of rate-dependent action on AERP and suggest that it may be possible to develop agents that have more desirable rate-dependent profiles than pure blockers of IKr.

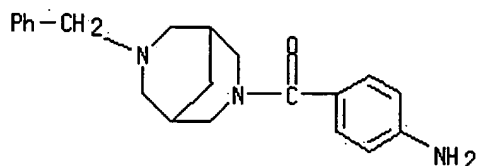
IT 83991-25-7, Ambasilide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(class III **antiarrhythmic** drug action in exptl. atrial fibrillation of sotalol and ambasilide)

RN 83991-25-7 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-aminobenzoyl)-7-(phenylmethyl)- (9CI)
(CA INDEX NAME)



L5 ANSWER 38 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1994:570198 HCAPLUS

DOCUMENT NUMBER: 121:170198

TITLE: Effects of novel **antiarrhythmic** agents, BRB-I-28 and its derivatives, on the heart mitochondrial respiratory chain and sarcoplasmic reticulum Ca²⁺-ATPase

AUTHOR(S): Chen, C. L.; Sangiah, S.; Yu, C.-A.; Chen, H.; Berlin, K. D.; Garrison, G. L.; Scherlag, B. J.; Lazzara, R.
CORPORATE SOURCE: Dep. Physiol. Sci., Oklahoma State Univ., Stillwater, OK, 74078, USA

SOURCE: Research Communications in Molecular Pathology and Pharmacology (1994), 85(2), 193-208
CODEN: RCMPE6; ISSN: 1078-0297

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of BRB-I-28 and its derivs. (GLG-V-13, SAZ-VII-22 and SAZ-VII-23), a novel group of **antiarrhythmic** agents, were investigated on the rat heart mitochondrial respiratory chain. The results indicate that BRB-I-28 and its derivs. have concn.-dependent inhibitory effects on NADH oxidase and NADH-CoQ reductase (complex I), but they have no significant effects on succinate oxidase, succinate dehydrogenase (complex II), CoQ-cytochrome c reductase (complex III), cytochrome c oxidase (complex IV), and NADH-K₃Fe(CN)₆ reductase. The site of inhibition of BRB-I-28 and its derivs. on the respiratory chain was localized between flavoprotein n (FPn) and CoQ, which is similar to the effect of rotenone and several other **antiarrhythmic** drugs such as amiodarone, propranolol, etc. BRB-I-28 and its derivs. also have significant inhibitory effects on mitochondrial ATPase activity as reported for other **antiarrhythmic** drugs such as amiodarone, propranolol, quinidine, and lidocaine.

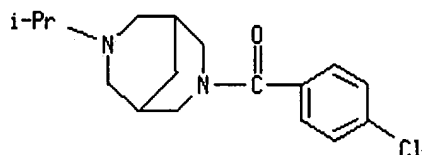
IT 129005-99-8, SAZ-VII 22

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**antiarrhythmic** agents BRB-I-28 and its derivs. effect on the heart mitochondrial respiratory chain and sarcoplasmic reticulum Ca²⁺-ATPase)

RN 129005-99-8 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-(4-chlorobenzoyl)-7-(1-methylethyl)-(9CI) (CA INDEX NAME)



L5 ANSWER 39 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1992:120648 HCAPLUS

DOCUMENT NUMBER: 116:120648

TITLE: Electrophysiological actions of a new **antiarrhythmic** drug, bisaramil, on isolated heart preparations
 AUTHOR(S): Paroczai, Margit; Karpati, Egon; Marko, Raisa; Kecskemeti, Valeria

CORPORATE SOURCE: Pharmacol. Res. Cent., Gedeon Richter Ltd., Budapest, H-1475, Hung.

SOURCE: Pharmacological Research (1992), 25(1), 75-85
 CODEN: PHMREP; ISSN: 1043-6618

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The electrophysiol. effects of bisaramil-a new **antiarrhythmic** drug under clin. trial-were investigated on isolated heart prepns., at a concn. range of $2.3-23 \times 10^{-6}$ M. Bisaramil dose dependently decreased the max. rate of depolarization (V_{max}), action potential amplitude (APA) and overshoot (OS) both in auricle and in papillary muscle of guinea-pig heart. There was no significant and obvious effect on the duration of the action potential and the resting membrane potential was also unchanged. Bisaramil slowed the spontaneous frequency of pacemaker cells in rabbit sinus node prepn. due to its inhibitory effect on slow diastolic depolarization (SDD). Bisaramil was able to inhibit slow Ca²⁺-action potentials induced by isoprenaline on K⁺-depolarized papillary muscle. Results obtained with transmembrane current measurements revealed that

bisaramil inhibited both fast Na⁺-current and slow Ca²⁺-current in frog sinoauricular fibers at the same concn. Bisaramil with a mixed mode of action seems to be a very promising drug.

IT **89194-77-4**, Bisaramil

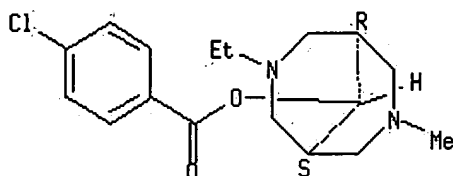
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**antiarrhythmic** activity of, mechanism of)

RN **89194-77-4** HCAPLUS

CN Benzoic acid, 4-chloro-, (9-syn)-3-ethyl-7-methyl-3,7-diazabicyclo[3.3.1]non-9-yl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



L5 ANSWER 40 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1991:647794 HCAPLUS

DOCUMENT NUMBER: 115:247794

TITLE: Electrophysiological properties of a new **antiarrhythmic** agent, bisaramil on guinea pig, rabbit and canine cardiac preparations

AUTHOR(S): Sunami, Akihiko; Sawanobori, Tohru; Adaniya, Hitoshi; Hiraoka, Masayasu

CORPORATE SOURCE: Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo, 113, Japan

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1991), 344(3), 323-30

CODEN: NSAPCC; ISSN: 0028-1298

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Electrophysiol. effects of bisaramil, a novel **antiarrhythmic** agent, were examd. using the conventional microelectrode technique applied to cardiac multicellular preps. from guinea-pigs, rabbits and dogs and the whole-cell patch-clamp technique applied to guinea-pig ventricular myocytes. Bisaramil at 10⁻⁶M or higher concns. produced a dose-dependent decrease in the max. rate of rise (.ovrhdot.V_{max}) of action potentials of guinea-pig papillary muscles without changes in resting membrane potentials. In the presence of bisaramil, trains of stimuli at rates >0.1 Hz led to the use-dependent block of .ovrhdot.V_{max}, which was enhanced at higher frequencies. At a concn. of 3 × 10⁻⁶M, the degree of use-dependent block was about 35% at 3.3 Hz, of which degree was comparable to those of 10⁻⁴M disopyramide and lidocaine. The development of .ovrhdot.V_{max} block by bisaramil was expressed by a single exponential function in the same manner as flecainide, whereas the time courses of the block development by disopyramide and lidocaine were described by two exponentials. Recovery time consts. from .ovrhdot.V_{max} block were 44.1 s and 20.3 s for bisaramil and flecainide, resp. Bisaramil at 10⁻⁶ and 3 × 10⁻⁶M did not change the action potential duration of guinea-pig papillary muscles and rabbit atrial muscles with a significant redn. of .ovrhdot.V_{max}. No change in action potential duration can be explained by depression of both the Ca²⁺ and the delayed outward K⁺ currents by

bisaramil. On the other hand, 10-6M bisaramil shortened action potential duration of canine Purkinje fibers at 50% and 90% of repolarization. In addn., bisaramil (3×10^{-6} M) suppressed sinus node automaticity, which agreed with voltage clamp studies indicating that bisaramil directly suppressed the calcium channel. These results suggest that bisaramil may be classified as class Ic agent showing a slow kinetic and potent action on the sodium channel.

IT 89194-77-4, Bisaramil

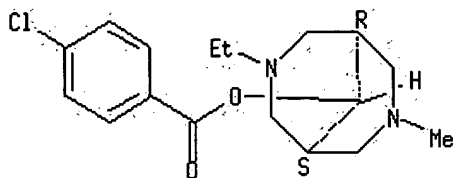
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(**antiarrhythmic** activity of, mechanism of)

RN 89194-77-4 HCAPLUS

CN Benzoic acid, 4-chloro-, (9-syn)-3-ethyl-7-methyl-3,7-diazabicyclo[3.3.1]non-9-yl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

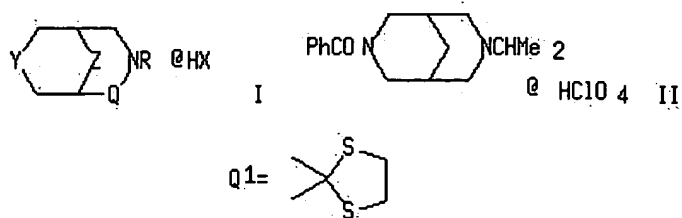


L5 ANSWER 41 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:	1991:514550 HCAPLUS
DOCUMENT NUMBER:	115:114550
TITLE:	Preparation of salts of 3-azabicyclo[3.3.1]nonanes as antiarrhythmic agents
INVENTOR(S):	Berlin, Kenneth Darrell; Scherlag, Benjamin Jacob; Clarke, Cyril Roy; Otiv, Surendra Kamchandra; Zisman, Stan Alan; Sangiah, Subbiah; Mulekar, Satish Vasant
PATENT ASSIGNEE(S):	Oklahoma State University, USA
SOURCE:	PCT Int. Appl., 68 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
<u>PATENT INFORMATION:</u>	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9107405	A1	19910530	WO 1990-US6625	19901113
W: JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5084572	A	19920128	US 1989-435976	19891113
US 5110933	A	19920505	US 1990-610428	19901107
<u>PRIORITY APPLN. INFO.:</u>			US 1989-435976	19891113
			US 1990-610428	19901107
OTHER SOURCE(S):	MARPAT 115:114550			
GI				



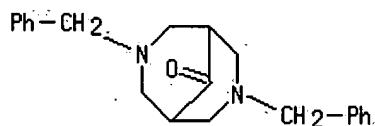
AB Title compds. [I; HX = pharmacol. acceptable acid; Q = CH₂, CO; Y = S, SO, CHCO₂Et, NR₁; Z = CH₂, CO, C(OMe)₂, Q₁; R = H, alkyl, (substituted) PhCH₂, PhCO; PhSO₂, Q₁; R₁ = alkyl, (substituted) PhCH₂, PhCO], were prepd. 7-Benzyl-3-isopropyl-3,7-diazabicyclo[3.3.1]nonane (prepn. from 1-isopropyl-4-piperidinone given) was refluxed with Pd/HCO₂NH₄ in MeOH to give the unprotected amine; the latter was acylated with PhCOCl in 10% NaOH/CH₂Cl₂ and the product was converted to perchlorate salt II. Several I at 3 mg/kg in dogs effectively eliminated induced ventricular tachycardia.

IT 59009-70-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as **antiarrhythmic**)

RN 59009-70-0 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonan-9-one, 3,7-bis(phenylmethyl)- (9CI) (CA
INDEX NAME)



L5 ANSWER 42 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
<p>1. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>2. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>3. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>4. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>5. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>6. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>7. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>8. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>9. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>10. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p>	<p>1. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>2. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>3. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>4. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>5. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>6. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>7. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>8. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>9. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p> <p>10. <i>Journal of the American Medical Association</i>. 2001;286:1206-1211.</p>

ACCESSION NUMBER: 1990:532149 HCAPLUS

DOCUMENT NUMBER: 113:132149

TITLE: A study of the synthesis and antiarrhythmic properties of selected 3,7-diheterabicyclo[3.3.1]nonanes with substituents at the 2,4-positions and at the 9-position

AUTHOR(S): Smith, Gary Steven; Thompson, Mark Daniel; Berlin, Kenneth Darrell; Holt, Elizabeth Manners; Scherlag, Benjamin Jacob; Patterson, Eugene; Lazzara, Ralph
CORPORATE SOURCE: Dep. Chem., Oklahoma State Univ., Stillwater, OK, 74078, USA

SOURCE: European Journal of Medicinal Chemistry (1990), 25(1), 1-8

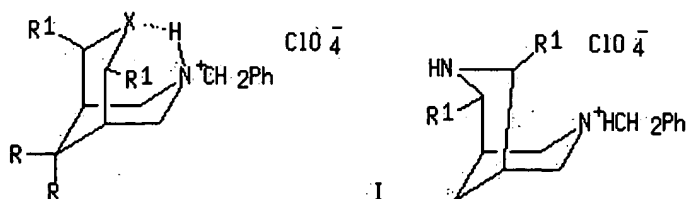
CODEN: EJMCA5; ISSN: 0223-5234

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S) : CASREACT 113:132149

GI



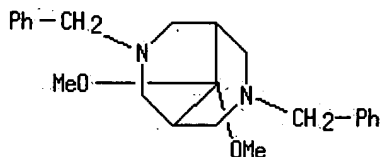
AB Some members of the family of 3,7-diheterabicyclo[3.3.1]nonanes I (X = S, R = OMe, R1 = H; X = NCH₂Ph, R = OH, OMe, R1 = H; X = NH, R = H, R1 = 2-ClC₆H₄) and II with substituents at the 2-, 4- and 9-positions were synthesized via Mannich reaction. Hearts of anesthetized dogs with myocardial infarctions were subjected to ventricular tachycardia (VT). I and II exhibited ability to abolish VT [or prevent the VT from being sustained] or reduce the rate of VT. A CH₂ group at the 9-position or the Me ketal group [(MeO)₂C(9)] enhanced the **antiarrhythmic** activity regardless of whether S or N was at 3-position. Compds. with aryl groups alpha to the heteroatoms were less effective in controlling VT. Lidocaine was the std.

IT **118958-16-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; **THU (Therapeutic use)**; **THU (Therapeutic use)**; USES (Uses)
(prepn. and **antiarrhythmic** activity of)

RN **118958-16-0** HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 9,9-dimethoxy-3,7-bis(phenylmethyl) - (9CI)
(CA INDEX NAME)



L5 ANSWER 43 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1990:515129 HCAPLUS

DOCUMENT NUMBER: 113:115129

TITLE: Part I. Synthesis and **antiarrhythmic** properties of substituted 3,7-diazabicyclo[3.3.1]nonanes and 3-azabicyclo[3.3.1]nonanes, and derivatives. Part II. Oxygen-17 NMR analysis of substituted 1-hetera-4-cyclohexanones

AUTHOR(S): Mulekar, Satish Vasant

CORPORATE SOURCE: Oklahoma State Univ., Stillwater, OK, USA

SOURCE: (1989) 181 pp. Avail.: Univ. Microfilms Int., Order No. DA9004033

From: Diss. Abstr. Int. B 1990, 50(9), 3997

DOCUMENT TYPE: Dissertation

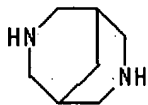
LANGUAGE: English

AB Unavailable

IT **280-74-0DP**, 3,7-Diazabicyclo[3.3.1]nonane, derivs.

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and **antiarrhythmic** activity of)

RN 280-74-0 HCAPLUS
 CN 3,7-Diazabicyclo[3.3.1]nonane (6CI, 8CI, 9CI) (CA INDEX NAME)

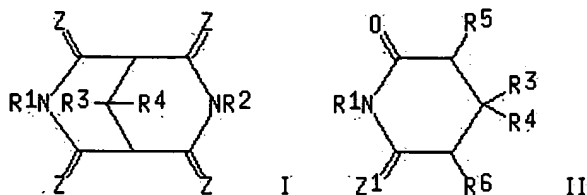


L5 ANSWER 44 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1990:198355 HCAPLUS
 DOCUMENT NUMBER: 112:198355
 TITLE: Preparation of 2,4,6,8-tetraoxo-3,7-diazabicyclo[3.3.1]nonanes as intermediates for antiarrhythmic agents
 INVENTOR(S): Schoen, Uwe; Hachmeister, Bernd; Kehrbach, Wolfgang; Kuhl, Ulrich; Buschmann, Gerd
 PATENT ASSIGNEE(S): Kali-Chemie Pharma G.m.b.H., Fed. Rep. Ger.
 SOURCE: Can., 52 pp. Division of Can. Appl. No. 436,831. CODEN: CAXXA4
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 1259998	A2	19890926	CA 1988-579322	19881004
DE 3234697	A1	19840322	DE 1982-3234697	19820918
CA 1254209	A1	19890516	CA 1983-436831	19830916
<u>PRIORITY APPLN. INFO.:</u>			DE 1982-3234697	19820918
			CA 1983-436831	19830916
OTHER SOURCE(S):		CASREACT 112:198355; MARPAT 112:198355		
GI				



AB The title compds. [I; Z = O; R1, R2 = H, C_≤12 alkyl, alkenyl, or alkynyl, C3-6 cycloalkyl or cycloalkylalkyl; R3, R4 = C1-7 alkyl; or R3R4 = (CH₂)_n; n = 3-6; provided that when R1 = R2 = H, R3 = R4 ≠ Me or R3R4 ≠ (CH₂)₃ or 5; when one of R1 and R2 = H and the other = Me or Et, only one of R3 and R4 = Me and R3R4 ≠ (CH₂)₃ or 5; when none of R1 and R2 = H, the substituents R1-R4 together contain at least 5 C atoms], useful as intermediates for antiarrhythmic I (Z = H₂) which reduce myocardial O consumption and affect heart rate, are prepd. by acid hydrolysis of oxopiperidinenitriles (II; Z1 = O, R5 = R6 = cyano; or Z1 = NH, R5 = cyano, R6 = N₂NCO) at 120-140° optionally followed by alkylation with R2X (X = leaving group; R2 ≠ H). Only general descriptions of the synthetic procedures are given. Twenty-seven I (Z = H₂) were prepd. by LiAlH₄ redn. of the corresponding I (Z = O). I (Z =

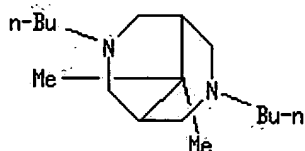
H2, R1 = R2 = Bu, R3 = R4 = Me) (III) at 13.5 $\mu\text{mol/kg}$ in an anesthetized rat lowered the heart rate from initial 372/min to 174/min, increased the systolic blood pressure from initial 104 mm Hg to 147 mm Hg, and reduced the double product (DP) by 36%. Tablet, capsule, and ampul formulations contg. III are given.

IT 90961-45-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as **antiarrhythmic**)

RN 90961-45-8 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3,7-dibutyl-9,9-dimethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 45 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1989:515218 HCAPLUS

DOCUMENT NUMBER: 111:115218

TITLE: Preparation and testing of bispidin derivatives as class III **antiarrhythmics**

INVENTOR(S): Lubisch, Wilfried; Binnig, Fritz; Von Philipsborn, Gerda

PATENT ASSIGNEE(S): BASF A.-G., Fed. Rep. Ger.

SOURCE: Eur. Pat. Appl., 12 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

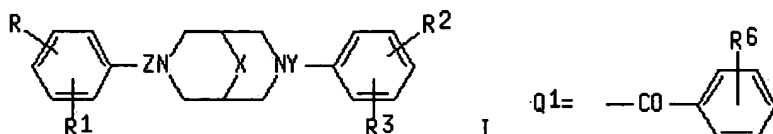
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 308843	A2	19890329	EP 1988-115299	19880917
EP 308843	A3	19900808		
EP 308843	B1	19931215		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
DE 3732094	A1	19890406	DE 1987-3732094	19870924
JP 01102078	A2	19890419	JP 1988-235124	19880921
US 4959373	A	19900925	US 1988-247645	19880922

PRIORITY APPLN. INFO.: DE 1987-3732094 19870924

OTHER SOURCE(S): CASREACT 111:115218; MARPAT 111:115218

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AB The title compds. (I; R, R1, R3 = H, C1-4 alkyl, halo, C1-4 alkoxy; R2 =

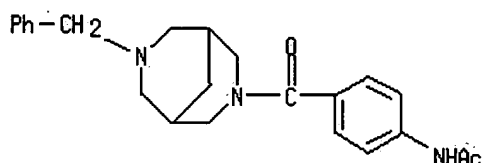
C1-4 alkyl halo, CN, C1-4 alkoxy NHS, 2Me, CF₃ NHCOMe, amino, NO₂; X = CH₂, CO, CR₄OR₅; R₄ = H, C1-4 alkyl; R₅ = R₄, Q1; R₆ = R₄, halo, C1-4 alkoxy; Y = CO, CONH; Z = C1-4 alkylene), were prepd. 3-(4-Aminobenzoyl)-7-benzyl-3,7-diazabicyclo[3.3.1]nonane in THF at ice temp. was treated with AcCl in THF and then with Et₃N at room temp. The mixt. was stirred overnight to give 3-(4-acetaminobenzoyl)-7-benzyl-3,7-diazabicyclo[3.3.1]nonane. I in guinea pigs showed prolongation of QT times with ED₂₀'s of 2.4-4.6 mg/kg i.v.

IT **122416-25-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as **antiarrhythmic**)

RN 122416-25-5 HCAPLUS

CN Acetamide, N-[4-[[7-(phenylmethyl)-3,7-diazabicyclo[3.3.1]non-3-yl]carbonyl]phenyl]- (9CI) (CA INDEX NAME)



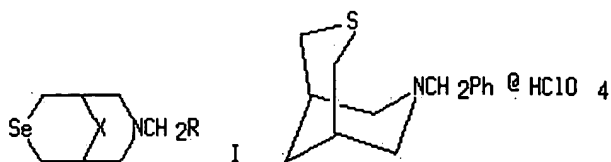
L5 ANSWER 46 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1989:95288 HCAPLUS
DOCUMENT NUMBER: 110:95288
TITLE: Preparation of 3-selena-7-azabicyclo[3.3.1]nonanes as **antiarrhythmic** agents
INVENTOR(S): Berlin, Kenneth D.; Thompson, Mark D.; Scherlag, Benjamin J.; Smith, Gary S.
PATENT ASSIGNEE(S): Oklahoma State University, USA
SOURCE: U.S., 24 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>US 4778892</u>	A	19881018	<u>US 1987-48325</u>	19870511
<u>US 4910311</u>	A	19900320	<u>US 1988-222057</u>	19880708
<u>US 4980468</u>	A	19901225	<u>US 1989-448658</u>	19891211
<u>US 5043445</u>	A	19910827	<u>US 1990-596550</u>	19901115
<u>US 5268481</u>	A	19931207	<u>US 1991-706215</u>	19910528
<u>PRIORITY APPLN. INFO.:</u>			<u>US 1987-48325</u>	19870511
			<u>US 1988-222057</u>	19880708
			<u>US 1989-448658</u>	19891211
			<u>US 1990-596550</u>	19901115

OTHER SOURCE(S): CASREACT 110:95288; MARPAT 110:95288
GI



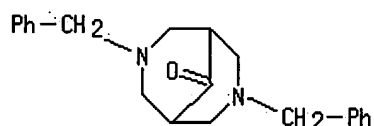
AB The title compds. [I; R = Ph, PhCH₂, 4-MeOC₆H₄CH₂, 3,4-(MeO)₂C₆H₃CH₂, 2-thienyl; X = CO, CH₂, C(OH)₂, C(OMe)₂] and their aza, oxa, and thia analogs and salts were prepd. as **antiarrhythmics**. PhCH₂NH₂, paraformaldehyde, HOAc, and 4-selenanone were refluxed in MeOH to give 43% exo-I (R = Ph, X = CO) which was heated 12 h at 140° with N₂H₄ in triethylene glycol to give, after acidification, 75% endo-I.HClO₄ (R = Ph, X = CH₂) (II). I reduce or eliminate artificially induced, sustained ventricular tachycardia in dogs at 3 and 6 mg/kg, their effect being superior to that of lidocaine.

IT **59009-70-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as **antiarrhythmic**)

RN **59009-70-0** HCAPLUS

CN **3,7-Diazabicyclo[3.3.1]nonan-9-one, 3,7-bis(phenylmethyl)-** (9CI) (CA INDEX NAME)



L5 ANSWER 47 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1984:455089 HCAPLUS
DOCUMENT NUMBER: 101:55089
TITLE: Diazabicyclo[3.3.1]nonanes
INVENTOR(S): Schoen, Uwe; Hachmeister, Bernd; Kehrbach, Wolfgang; Kuehl, Ulrich; Buschmann, Gerd
PATENT ASSIGNEE(S): Kali-Chemie Pharma G.m.b.H., Fed. Rep. Ger.
SOURCE: Ger. Offen., 30 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

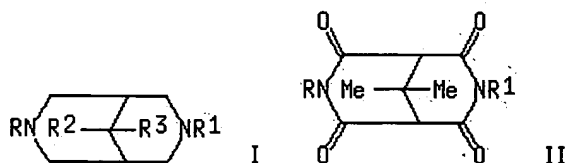
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3234697	A1	19840322	DE 1982-3234697	19820918
ZA 8306185	A	19840425	ZA 1983-6185	19830822
JP 59070686	A2	19840421	JP 1983-154236	19830825
JP 05037150	B4	19930602		
DD 213923	A5	19840926	DD 1983-254711	19830909
EP 103833	A2	19840328	EP 1983-108990	19830912
EP 103833	A3	19841128		
EP 103833	B1	19890816		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
EP 250903	A2	19880107	EP 1987-108007	19830912

EP 250903	A3	19880309		
EP 250903	B1	19911127		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 45579	E	19890915	AT 1983-108990	19830912
AT 69817	E	19911215	AT 1987-108007	19830912
HU 32114	O	19840628	HU 1983-3182	19830914
HU 191096	B	19870128		
DK 8304225	A	19840319	DK 1983-4225	19830916
DK 165833	B	19930125		
DK 165833	C	19930621		
NO 8303346	A	19840319	NO 1983-3346	19830916
NO 160516	B	19890116		
NO 160516	C	19890426		
AU 8319206	A1	19840322	AU 1983-19206	19830916
AU 564910	B2	19870903		
ES 525653	A1	19840601	ES 1983-525653	19830916
US 4550112	A	19851029	US 1983-532762	19830916
IL 69751	A1	19861031	IL 1983-69751	19830916
SU 1272989	A3	19861123	SU 1983-3646751	19830916
CA 1254209	A1	19890516	CA 1983-436831	19830916
FI 8303339	A	19840319	FI 1983-3339	19830919
FI 76338	B	19880630		
FI 76338	C	19881010		
US 4742172	A	19880503	US 1987-54868	19870527
CA 1259998	A2	19890926	CA 1988-579322	19881004
JP 05247039	A2	19930924	JP 1991-308735	19911125
JP 06070056	B4	19940907		

PRIORITY APPLN. INFO.:

DE 1982-3234697	19820918
EP 1983-108990	19830912
EP 1987-108007	19830912
CA 1983-436831	19830916
US 1983-532762	19830916
US 1985-759351	19850726

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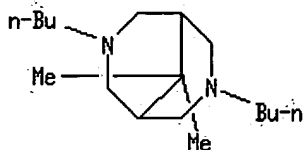
AB 3,7-Diazabicyclononanes I (R,R1 = alkyl, alkenyl, alkynyl; R2,R3 = alkyl; R2R3 = alkylene), useful as antiarrhythmics, were prepd. Thus, 4,4-dimethyl-2,6-dioxo-3,5-piperidinedicarbonitrile was hydrolyzed and cyclized by heating in H₂SO₄ to give tetrone II (R = R1 = H). The last was alkylated with BuBr to give II (R = R1 = Bu) which was reduced with LiAlH₄ to give I (R = R1 = Bu, R2 = R3 = Me) (III). In rats 13.5 µmol III/kg i.v. reduced heart frequency from 372/min to 174/min while increasing systolic blood pressure from 104 to 147 mm Hg.

IT 90961-45-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. and antiarrhythmic activity of)

RN 90961-45-8 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3,7-dibutyl-9,9-dimethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 48 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

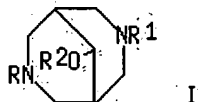
Full Text	Citing References
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ACCESSION NUMBER: 1983:405654 HCAPLUS
 DOCUMENT NUMBER: 99:5654
 TITLE: Bicyclic compounds and pharmaceutical compositions containing them
 PATENT ASSIGNEE(S): Richter, Gedeon, Vegyeszeti Gyar Rt. , Hung.
 SOURCE: Belg., 30 pp.
 CODEN: BEXXAL
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>BE 893891</u>	A1	19830120	<u>BE 1982-208636</u>	19820720
<u>HU 26161</u>	O	19830928	<u>HU 1981-2112</u>	19810720
<u>HU 184960</u>	B	19841128		
<u>ZA 8204809</u>	A	19830427	<u>ZA 1982-4809</u>	19820706
<u>IL 66277</u>	A1	19850830	<u>IL 1982-66277</u>	19820708
<u>AT 8202723</u>	A	19850715	<u>AT 1982-2723</u>	19820713
<u>AT 379809</u>	B	19860310		
<u>CA 1254208</u>	A1	19890516	<u>CA 1982-407149</u>	19820713
<u>FI 8202526</u>	A	19830121	<u>FI 1982-2526</u>	19820715
<u>FI 71320</u>	B	19860909		
<u>FI 71320</u>	C	19861219		
<u>CH 653032</u>	A	19851213	<u>CH 1982-4315</u>	19820715
<u>DK 8203199</u>	A	19830121	<u>DK 1982-3199</u>	19820716
<u>DK 160875</u>	B	19910429		
<u>DK 160875</u>	C	19911014		
<u>DD 202575</u>	A5	19830921	<u>DD 1982-241725</u>	19820716
<u>US 4451473</u>	A	19840529	<u>US 1982-398801</u>	19820716
<u>NO 8202485</u>	A	19830121	<u>NO 1982-2485</u>	19820719
<u>NO 157421</u>	B	19871207		
<u>NO 157421</u>	C	19880316		
<u>SE 8204393</u>	A	19830121	<u>SE 1982-4393</u>	19820719
<u>SE 450704</u>	B	19870720		
<u>SE 450704</u>	C	19871029		
<u>AU 8286176</u>	A1	19830127	<u>AU 1982-86176</u>	19820719
<u>AU 552770</u>	B2	19860619		
<u>FR 2510575</u>	A1	19830204	<u>FR 1982-12572</u>	19820719
<u>FR 2510575</u>	B1	19860207		
<u>GB 2102801</u>	A1	19830209	<u>GB 1982-20818</u>	19820719
<u>GB 2102801</u>	B2	19850327		
<u>DE 3226921</u>	A1	19830210	<u>DE 1982-3226921</u>	19820719
<u>DE 3226921</u>	C2	19940310		
<u>NL 8202908</u>	A	19830216	<u>NL 1982-2908</u>	19820719
<u>JP 58049383</u>	A2	19830323	<u>JP 1982-125600</u>	19820719
<u>JP 03052465</u>	B4	19910812		
<u>ES 514126</u>	A1	19840101	<u>ES 1982-514126</u>	19820719

<u>CS 235302</u>	B2	19850515	<u>CS 1982-5520</u>	19820719
<u>SU 1222197</u>	A3	19860330	<u>SU 1982-3465423</u>	19820719
<u>IN 155994</u>	A	19850420	<u>IN 1982-CA832</u>	19820720
<u>PL 135878</u>	B1	19851231	<u>PL 1982-237566</u>	19820720
<u>PL 135814</u>	B1	19851231	<u>PL 1982-244329</u>	19820720
<u>ES 520567</u>	A1	19840501	<u>ES 1983-520567</u>	19830314
<u>CS 235316</u>	B2	19850515	<u>CS 1983-1747</u>	19830314
<u>SU 1272990</u>	A3	19861123	<u>SU 1983-3646755</u>	19830922
<u>IN 160649</u>	A	19870725	<u>IN 1984-MA369</u>	19840521
<u>AT 8403349</u>	A	19850715	<u>AT 1984-3349</u>	19841019
<u>AT 379810</u>	B	19860310		
<u>PRIORITY APPLN. INFO.:</u>			<u>HU 1981-2112</u>	19810720
			<u>AT 1982-2723</u>	19820713
			<u>CS 1982-5520</u>	19820719
			<u>IN 1982-CA832</u>	19820720

OTHER SOURCE(S): CASREACT 99:5654
GI



AB The diazabicyclononanols I (R, R1 = alkyl; R2 = CH2Ph, CHPh2, Ph, substituted Ph, acyl) (~70 compds.) were prepd. Thus I (R = R1 = Me, R2 = H) prepd. by reducing the ketone, was treated with BzCl to give I (R = R1 = Me, R2 = Bz) which has an **antiarrhythmic** ED50 of 0.08 mg/kg i.v. in rats. I also have local anesthetic activity comparable to that of lidocaine and Ca blocking activity.

IT **85927-72-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. and **antiarrhythmic** activity of)

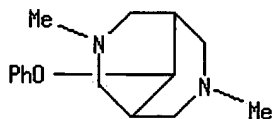
RN **85927-72-6** HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3,7-dimethyl-9-phenoxy-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN **85927-71-5**

CMF C15 H22 N2 O

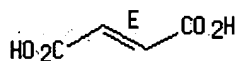


CM 2

CRN **110-17-8**

CMF C4 H4 O4

Double bond geometry as shown.



L5 ANSWER 49 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1979:501880 HCAPLUS
 DOCUMENT NUMBER: 91:101880
 TITLE: **Antiarrhythmic activity of some N-alkylbispidinebenzamides**
 AUTHOR(S): Ruenitz, Peter C.; Mokler, Corwin M.
 CORPORATE SOURCE: Sch. Pharm., Univ. Georgia, Athens, GA, 30602, USA
 SOURCE: Journal of Medicinal Chemistry (1979), 22(9), 1142-4
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Nine bispidinebenzamides I (R = Me or Bu; R1 = H, OMe, or Cl; n = 1, 2, or 3; X = HCl or fumarate) were synthesized by condensation of N-methyl- [58324-99-5] or N-butylbispidine [58325-01-2] with the appropriate acid chlorides. The synthesized compds. were evaluated in mice for acute toxicity and their ability to protect against chloroform-induced ventricular fibrillation. All of them were active. I; R = Me, R1 = H, X = fumarate [70802-37-8], I; R = Me, R1 = 4-MeO, X = fumarate [70802-39-0], and I; R = Me, R1 = 4-Cl, X = fumarate [71004-34-7] had potencies and LD50-to-ED50 ratios comparable to those of disopyramide. However, their potencies in increasing the effective refractory period in isolated rabbit atria were considerably less than that of disopyramide.

IT 70802-25-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. and **antiarrhythmic** activity of)

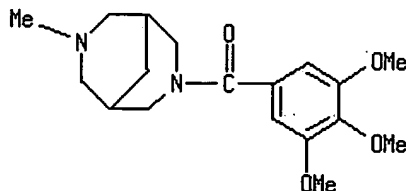
RN 70802-25-4 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-methyl-7-(3,4,5-trimethoxybenzoyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 70802-24-3

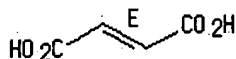
CMF C18 H26 N2 O4



CM 2

CRN 110-17-8
CMF C4 H4 O4

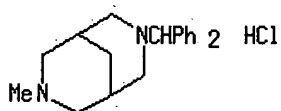
Double bond geometry as shown.



L5 ANSWER 50 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1977:577686 HCAPLUS
DOCUMENT NUMBER: 87:177686
TITLE: Analogs of sparteine. 5. **Antiarrhythmic** activity of selected N,N'-disubstituted bispidines
AUTHOR(S): Ruenitz, Peter C.; Mokler, Corwin M.
CORPORATE SOURCE: Sch. Pharm., Univ. Georgia, Athens, GA, USA
SOURCE: Journal of Medicinal Chemistry (1977), 20(12), 1668-71
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



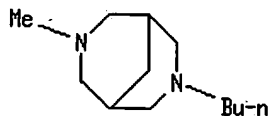
AB Seven title compds., inner ring analogs of sparteine, were tested for **antiarrhythmic** potency by the mouse-chloroform fibrillation assay and for acute toxicity in mice. Several compds. had **antiarrhythmic** potency comparable to sparteine, but were somewhat less toxic.
N-benzhydryl-N'-methylbispidine-HCl (I) [64304-24-1] was prepd. by the cyclization reaction of N-methyl-4-piperidone [1445-73-4] with benzhydrylamine [91-00-9] and paraformaldehyde followed by reaction with alk. NH₂NH₂. Activity-lipophilicity (partition coeff.) relations are discussed. Sparteine and 2 title analogs showed no signs of binding of Ca²⁺ or Mg²⁺ as detd. by NMR anal.

IT **58324-88-2**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; **THU (Therapeutic use)**; USES (Uses)
(**antiarrhythmic** activity of)

RN 58324-88-2 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3-butyl-7-methyl-, monohydrobromide (9CI)
(CA INDEX NAME)



HBr

L5 ANSWER 51 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1976:150675 HCAPLUS
 DOCUMENT NUMBER: 84:150675
 TITLE: **Antiarrhythmic** bispidin derivatives
 INVENTOR(S): Binnig, Fritz; Raschack, Manfred; Treiber, Hans J.
 PATENT ASSIGNEE(S): Knoll A.-G. Chemische Fabriken, Fed. Rep. Ger.
 SOURCE: Ger. Offen., 19 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2428792	A1	19760102	DE 1974-2428792	19740614
GB 1445967	A	19760811	GB 1975-21379	19750520
FR 2274300	A1	19760109	FR 1975-16828	19750529
FR 2274300	B1	19781110		
FI 7501726	A	19751215	FI 1975-1726	19750610
FI 57759	B	19800630		
FI 57759	C	19801010		
NL 7506886	A	19751216	NL 1975-6886	19750610
US 3962449	A	19760608	US 1975-585606	19750610
BE 830153	A1	19751212	BE 1975-157260	19750612
SE 7506743	A	19751215	SE 1975-6743	19750612
SE 420727	B	19811026		
SE 420727	C	19820204		
AT 7504514	A	19771015	AT 1975-4514	19750612
JP 51011791	A2	19760130	JP 1975-71827	19750613
CA 1058181	A1	19790710	CA 1975-229274	19750613
CH 618168	A	19800715	CH 1975-7712	19750613
PRIORITY APPLN. INFO.:			DE 1974-2428792	19740614

GI



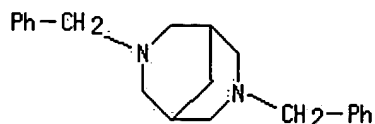
AB Bispidine derivs. I (R = Me, R1 = hexyl, CH2Ph, CHPh2, (CH2)3CHPh2; R = R1 = CH2Ph; R = CHMe2, CH2CH2Ph, R1 = CH2CH2Ph; X = H2) were prepd. by treating the piperidinone II with R1NH2 and CH2O, and hydrazinolysis of I (X = O), or by debenzylating I (R = Me, R1 = CH2Ph) and alkylation with appropriate alkyl halides. I (R = R1 = CH2Ph) had an antiarrhythmic ED25 of 0.034 in the isolated guinea pig atrium test and an **antiarrhythmic-inotropic** therapeutic index of 2.0.

IT 59009-71-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. and **antiarrhythmic** activity of)

RN 59009-71-1 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane, 3,7-bis(phenylmethyl) - (9CI) (CA INDEX NAME)



L5 ANSWER 52 OF 52 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1969:85991 HCAPLUS
 DOCUMENT NUMBER: 70:85991
 TITLE: **Antiarrhythmic** activity of some 1,5- \square diphenylbispidine derivatives
 AUTHOR(S): Rossi Cartoni, Carla; Figini, Alberto; Carpi, Amilcare
 CORPORATE SOURCE: Lab. Chim. Ter., Ist. Super. Sanita, Rome, Italy
 SOURCE: Annali dell'Istituto Superiore di Sanita (1968), 4(3-4), 333-5
 CODEN: AISSAW; ISSN: 0021-2571
 DOCUMENT TYPE: Journal
 LANGUAGE: Italian

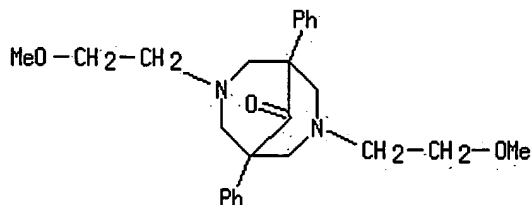
AB The **antiarrhythmic** activity of title compds. was investigated in dogs, in vivo, and on the rabbit auricle, in vitro. The activity of 1,5-diphenyl-3,7-bis(.beta.-diethylaminoethyl)bispidin-9-ol (I), as compared to that of quinidine (II), was much higher in vivo, and much lower in vitro. The in vivo activity of 1,5-diphenyl-3,7-di(R- \square substituted)bispidin-9-one [R = CH₂CH₂OMe, (CH₂)₃OMe, CMe₂CH₂OH and (CH₂)₃OH] was between that of I and II. The toxicity in guinea pigs was in the order: I .ltoreq. III (R = CH₂CH₂OMe) < III [R = (CH₂)₃OMe] < III (= CMe₂CH₂OH) < II < III [R = (CH₂)₃OH].

IT 4208-23-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (antiarrhythmic activity of)

RN 4208-23-5 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonan-9-one, 3,7-bis(2-methoxyethyl)-1,5-diphenyl-(7CI, 8CI, 9CI) (CA INDEX NAME)



=> file reg

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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DICTIONARY FILE UPDATES: 30 MAR 2004 HIGHEST RN 669048-54-8

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<http://www.cas.org/ONLINE/DBSS/registryss.html>

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L6 STRUCTURE UPLOADED

=> d 16

L6 HAS NO ANSWERS

L6 STR

=> s 16

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SAMPLE SCREEN SEARCH COMPLETED - 65 TO ITERATE

100.0% PROCESSED 65 ITERATIONS
SEARCH TIME: 00.00.01

8 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 817 TO 1783
PROJECTED ANSWERS: 8 TO 329

L7 8 SEA SSS SAM L6

=> s 16 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 18:46:59 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1296 TO ITERATE

100.0% PROCESSED 1296 ITERATIONS
SEARCH TIME: 00.00.01

142 ANSWERS

L8 142 SEA SSS FUL L6

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	156.68	580.24
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-35.34

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FILE COVERS 1907 - 31 Mar 2004 VOL 140 ISS 14
 FILE LAST UPDATED: 30 Mar 2004 (20040330/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 18

L9 20 L8

=> s 19 and bjorsne, m?/au

5 BJORSNE, M?/AU

L10 4 L9 AND BJORSNE, M?/AU

=> d 110, ibib abs fhitr, 1-4

L10 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
--------------	----------------------

ACCESSION NUMBER:	2000:900637 HCAPLUS
DOCUMENT NUMBER:	134:56700
TITLE:	Preparation of new bispindines useful in the treatment of cardiac arrhythmias
INVENTOR(S):	Alstermark, Christer; Andersson, Kjell; Bjore, Annika; Bjorsne, Magnus ; Lindstedt, Alstermark Eva-Lotte; Nilsson, Goran; Polla, Magnus; Strandlund, Gert; Ortengren, Ylva
PATENT ASSIGNEE(S):	Astrazeneca AB, Swed.
SOURCE:	PCT Int. Appl., 130 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
<u>PATENT INFORMATION:</u>	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077000	A1	20001221	WO 2000-SE1254	20000615
WO 2000077000	C2	20030619		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 2000011660 A 20020326 BR 2000-11660 20000615

EP 1192157 A1 20020403 EP 2000-946589 20000615

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2003502329 T2 20030121 JP 2001-503858 20000615

EE 200100675 A 20030217 EE 2001-675 20000615

AU 761576 B2 20030605 AU 2000-60324 20000615

NZ 516013 A 20030630 NZ 2000-516013 20000615

ZA 2001009796 A 20030228 ZA 2001-9796 20011128

NO 2001006117 A 20020215 NO 2001-6117 20011214

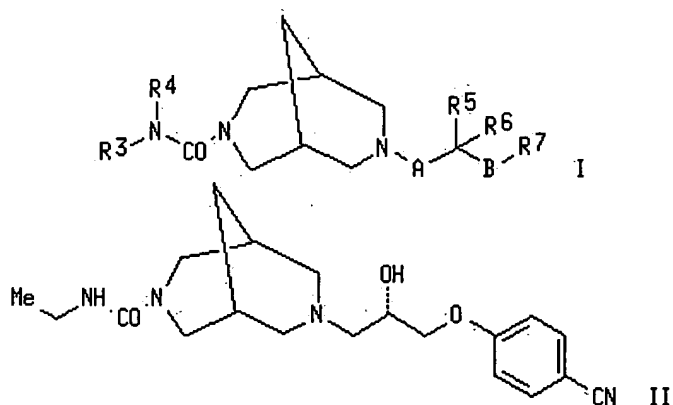
PRIORITY APPLN. INFO.:

SE 1999-2268 A 19990616

WO 2000-SE1254 W 20000615

OTHER SOURCE(S): MARPAT 134:56700

GI



AB Bispidines, such as I [R3 = H, alkyl; R4 = H, alkyl, alkoxy; NR3R4 = heterocyclyl; R5 = H, halogen, alkyl, alkoxy, acyloxy, alkylsulfonyloxy, carbamoyl, etc.; R6 = H, alkyl; R5R6 = O; R7 = alkyl, aryl, heterocyclyl; A, B = bond, linking group, such as alkylene, etc.], were prepd. for pharmaceutical use in the treatment of cardiac arrhythmias, in particular atrial and ventricular arrhythmias. Thus, bispidine II was prepd. with 51% yield by amidation of (S)-4-[3-(3,7-diazabicyclo[3.3.1]non-3-yl)-2-hydroxypropoxy]benzonitrile with Et isocyanate. The prepd. bispidines were tested for primary electrophysiol. effects in anesthetized guinea pigs.

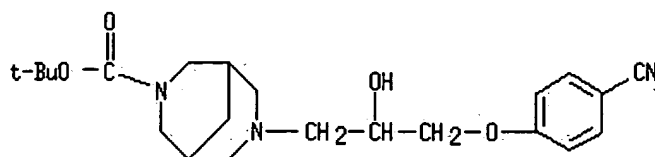
IT 227939-99-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of new bispidines useful in the treatment of cardiac arrhythmias)

RN 227939-99-3 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[3-(4-cyanophenoxy)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



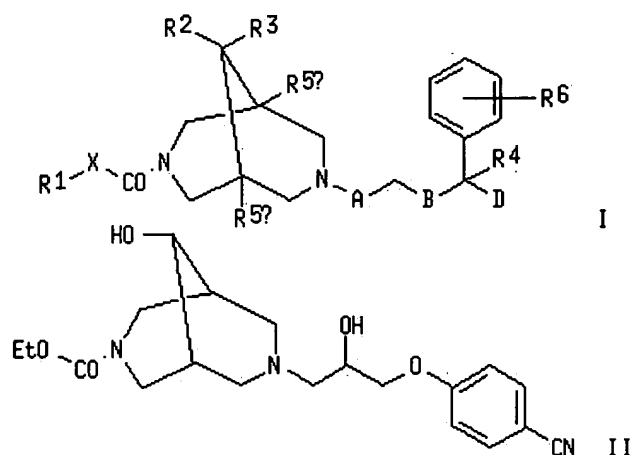
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2000:900636 HCAPLUS
DOCUMENT NUMBER: 134:42151
TITLE: Preparation of new bispidines useful in the treatment of cardiac arrhythmias
INVENTOR(S): Bjore, Annika; Bjorsne, Magnus; Halvarsson, Torbjorn; Hoffmann, Kurt-jurgen; Samuelsson, Bertil; Strandlund, Gert
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 2000076999</u>	A1	20001221	<u>WO 2000-SE1253</u>	20000615
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, VZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
<u>BR 2000011673</u>	A	20020312	<u>BR 2000-11673</u>	20000615
<u>EP 1192154</u>	A1	20020403	<u>EP 2000-944526</u>	20000615
<u>EP 1192154</u>	B1	20040317		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
<u>JP 2003502328</u>	T2	20030121	<u>JP 2001-503857</u>	20000615
<u>EE 200100674</u>	A	20030217	<u>EE 2001-674</u>	20000615
<u>AU 762244</u>	B2	20030619	<u>AU 2000-58611</u>	20000615
<u>NZ 516015</u>	A	20030630	<u>NZ 2000-516015</u>	20000615
<u>ZA 2001009800</u>	A	20030228	<u>ZA 2001-9800</u>	20011128
<u>NO 2001006127</u>	A	20020212	<u>NO 2001-6127</u>	20011214
PRIORITY APPLN. INFO.:				
			<u>SE 1999-2270</u>	A 19990616
			<u>WO 2000-SE1253</u>	W 20000615
OTHER SOURCE(S): MARPAT 134:42151				
GI				



AB Bispidines, such as I [R1 = alkyl, arylalkyl, etc.; R2, R3 = H, OH, alkyl, etc.; R2R3 = O; R4, R5a, R5b = H, alkyl; R6 = OH, CN, NO2, NH2, halogen, etc.; X = O, S; A, B = bond, linking group, such as alkylene, etc.; D = H, OH, alkyl, aminoalkyl, etc.], were prepd. for pharmaceutical use in the treatment of cardiac arrhythmias, in particular atrial and ventricular arrhythmias. Thus, bispidine II was prepd. in multistep synthetic sequence starting from Et 4-oxo-1-piperidinecarboxylate, epichlorohydrin, and 4-cyanophenol. The prepd. bispidines were tested for primary electrophysiol. effects in anesthetized guinea pigs.

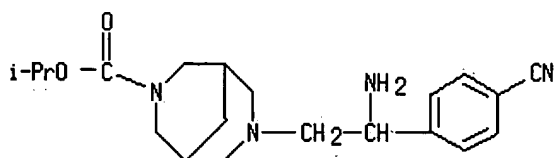
IT **313238-19-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of new bispidines useful in the treatment of cardiac arrhythmias)

RN **313238-19-6 HCAPLUS**

CN **3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[2-amino-2-(4-cyanophenyl)ethyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)**



REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2000:900635 HCAPLUS

DOCUMENT NUMBER: 134:42150

TITLE: Preparation of new bispidines useful in the treatment of cardiac arrhythmias

INVENTOR(S): Bjorsne, Magnus; Frantsi, Marianne; Hoffmann, Kurt-Jurgen; Ohlsson, Bengt

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 76 pp.

CODEN: PIXXD2

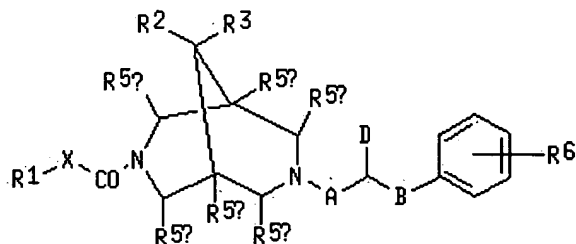
DOCUMENT TYPE: Patent

LANGUAGE: English

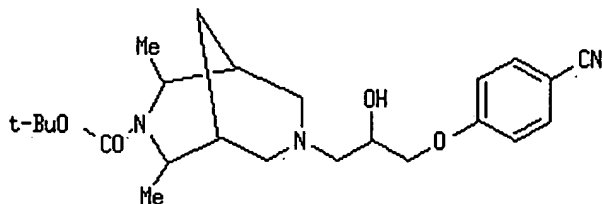
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076998	A1	20001221	WO 2000-SE1252	20000615
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000011667	A	20020402	BR 2000-11667	20000615
EP 1192156	A1	20020403	EP 2000-946588	20000615
EP 1192156	B1	20040218		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003502327	T2	20030121	JP 2001-503856	20000615
EE 200100679	A	20030217	EE 2001-679	20000615
AU 762040	B2	20030619	AU 2000-60323	20000615
NZ 516014	A	20030630	NZ 2000-516014	20000615
ZA 2001009798	A	20030228	ZA 2001-9798	20011128
NO 2001006120	A	20020218	NO 2001-6120	20011214
<u>PRIORITY APPLN. INFO.:</u>			SE 1999-2269	A 19990616
			WO 2000-SE1252	W 20000615
OTHER SOURCE(S): MARPAT 134:42150				
GI				



I



II

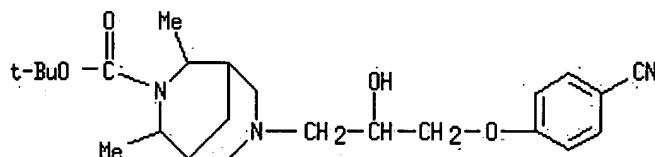
AB Bispidines, such as I [R1 = alkyl, arylalkyl, etc.; R2, R3, R5a, R5b, R5c, R5d, R5e, R5f = H, alkyl; R6 = OH, CN, NO2, NH2, halogen, etc.; R9 = alkyl, aryl, acyl, etc.; X = O, S; A, B = bond, linking group, such as alkylene, etc.; D = OH, alkyl, etc.], were prep'd. for pharmaceutical use in the treatment of cardiac arrhythmias, in particular atrial and ventricular arrhythmias. Thus, bispidine II was prep'd. in multistep synthetic sequence starting from N,N'-dibenzylbispidine, 4-cyanophenol, and epichlorohydrin. The prep'd. bispidines were tested for primary electrophysiol. effects in anesthetized guinea pigs.

IT 312961-89-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of new bispindines useful in the treatment of cardiac arrhythmias)

RN 312961-89-0 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[3-(4-cyanophenoxy)-2-hydroxypropyl]-2,4-dimethyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1999:404964 HCAPLUS

DOCUMENT NUMBER: 131:58860

TITLE: Preparation of 3,7-diazabicyclo[3.3.1]nonane-3-carboxylates as antiarrhythmic agents

INVENTOR(S): Strandlund, Gert; Alstermark, Christer; Bjore, Annika; Bjorsne, Magnus; Frantsi, Marianne; Halvarsson, Torbjorn; Hoffmann, Kurt-Jurgen; Lindstedt, Eva-Lotte; Polla, Magnus

PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.

SOURCE: PCT Int. Appl., 129 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

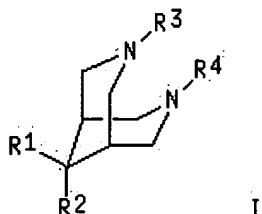
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931100	A1	19990624	WO 1998-SE2276	19981210
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9811130	A	19990617	ZA 1998-11130	19981204
CA 2314490	AA	19990624	CA 1998-2314490	19981210
AU 9917953	A1	19990705	AU 1999-17953	19981210
BR 9813668	A	20001017	BR 1998-13668	19981210
EP 1047695	A1	20001102	EP 1998-962796	19981210
EP 1047695	B1	20040317		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

EE 200000365	A	20011015	EE 2000-200000365	19981210
JP 2002508375	T2	20020319	JP 2000-539024	19981210
US 6291475	B1	20010918	US 1999-214756	19990112
NO 2000003137	A	20000817	NO 2000-3137	20000616
PRIORITY APPLN. INFO.:			SE 1997-4709	A 19971217
			WO 1998-SE2276	W 19981210

OTHER SOURCE(S): MARPAT 131:58860

GI



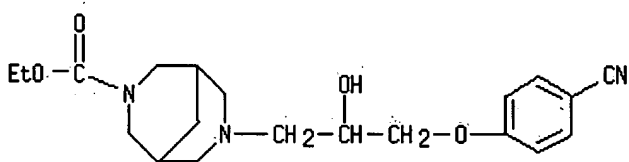
AB Title compds. [I; R1,R2 = H or alkyl; R1R2 = OCH2CH2O, (CH2)4-5; R3 = CCR10R11AR; A = bond, alkylene, (CH2)nZ, CONR20, etc.; B = bond, alkylene, NR23(CH2)r, O(CH2)r; R = (un)substituted Ph; R4 = COXR9; R9 = alkyl, (un)substituted phenyl(alkyl), -naphthyl; R10 = H or OH; R11,R20,R23 = H or alkyl; X = O or S; Z = NR20, SO0-2, O; n,r = 0-4] were prepd. Thus, 4-(NC)C6H4OH was condensed with epichlorohydrin and the product aminated by I (R1 = R2 = H, R4 = CO2CMe3) (II; R3 = H) (prepn. given) to give II [R3 = CH2CH(OH)CH2OC6H4(CN)-4]. Data for biol. activity of I were given.

IT 227939-98-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3,7-diazabicyclo[3.3.1]nonane-3-carboxylates as antiarrhythmic agents)

RN 227939-98-2 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[3-(4-cyanophenoxy)-2-hydroxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 18:37:29 ON 31 MAR 2004)

FILE 'REGISTRY' ENTERED AT 18:37:34 ON 31 MAR 2004

L1 STRUCTURE UPLOADED

L2 50 S L1

L3 2733 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 18:39:23 ON 31 MAR 2004

L4 86 S L3/THU

L5 52 S L4 AND ?ARRHYTHM?

FILE 'REGISTRY' ENTERED AT 18:44:53 ON 31 MAR 2004

L6 STRUCTURE UPLOADED

L7 8 S L6

L8 142 S L6 FULL

FILE 'HCAPLUS' ENTERED AT 18:47:02 ON 31 MAR 2004

L9 20 S L8

L10 4 S L9 AND BJORSNE, M?/AU

=> s l9 not l10

L11 16 L9 NOT L10

=> s l11 and frantsi, m?/au

6 FRANTSI, M?/AU

L12 1 L11 AND FRANTSI, M?/AU

=> s l12 not l10

L13 1 L12 NOT L10

=> d l13, ibib abs fhitr, 1

L13 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2000:900634 HCAPLUS

DOCUMENT NUMBER: 134:42149

TITLE: Preparation of new bispindines useful in the treatment of cardiac arrhythmias

INVENTOR(S): **Frantsi, Marianne**; Hoffmann, Kurt-Jurgen; Strandlund, Gert

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

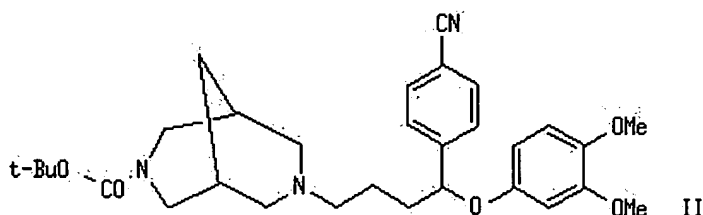
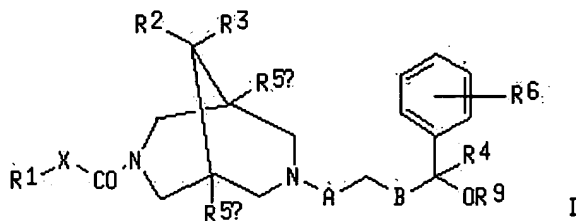
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076997	A1	20001221	WO 2000-SE1251	20000615
W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
BR 2000011675	A	20020319	BR 2000-11675	20000615
EP 1192155	A1	20020403	EP 2000-946587	20000615
EP 1192155	B1	20030402		
R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO		
JP 2003502326	T2	20030121	JP 2001-503855	20000615
EE 200100678	A	20030217	EE 2001-678	20000615
AT 236159	E	20030415	AT 2000-946587	20000615
NZ 516016	A	20030630	NZ 2000-516016	20000615
US 6465481	B1	20021015	US 2000-623707	20000907

ZA 2001009858	A	20030228	ZA 2001-9858	20011129
NO 2001006119	A	20020211	NO 2001-6119	20011214
PRIORITY APPLN. INFO.:			SE 1999-2271	A 19990616
			WO 2000-SE1251	W 20000615
OTHER SOURCE(S):			CASREACT 134:42149; MARPAT 134:42149	
GI				



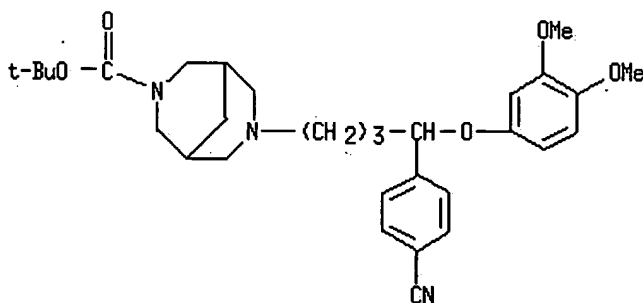
AB Bispidines, such as I [R1 = alkyl, arylalkyl, etc.; R2, R3, R4, R5a, R5b = H, alkyl; R6 = OH, CN, NO2, NH2, halogen, etc.; R9 = alkyl, aryl, acyl, etc.; X = O, S; A, B = bond, linking group, such as alkylene, etc.], were prepd. for pharmaceutical use in the treatment of cardiac arrhythmias, in particular atrial and ventricular arrhythmias. Thus, bispidine II was prepd. in multistep synthetic sequence starting from N,N'-dibenzylbispidine, 4-(1-hydroxy-3-butenyl)benzonitrile, and 3,4-dimethoxyphenol. The prepd. bispidines were tested for primary electrophysiol. effects in anesthetized guinea pigs.

IT **312955-28-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bispidines useful in the treatment of cardiac arrhythmias)

RN **312955-28-5 HCAPLUS**

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[4-(4-cyanophenyl)-4-(3,4-dimethoxyphenoxy)butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 18:37:29 ON 31 MAR 2004)

FILE 'REGISTRY' ENTERED AT 18:37:34 ON 31 MAR 2004

L1 STRUCTURE UPLOADED
L2 50 S L1
L3 2733 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 18:39:23 ON 31 MAR 2004

L4 86 S L3/THU
L5 52 S L4 AND ?ARRHYTHM?

FILE 'REGISTRY' ENTERED AT 18:44:53 ON 31 MAR 2004

L6 STRUCTURE UPLOADED
L7 8 S L6
L8 142 S L6 FULL

FILE 'HCAPLUS' ENTERED AT 18:47:02 ON 31 MAR 2004

L9 20 S L8
L10 4 S L9 AND BJORSNE, M?/AU
L11 16 S L9 NOT L10
L12 1 S L11 AND FRANTSI, M?/AU
L13 1 S L12 NOT L10

=> s l9 and hoffman, k?/au

598 HOFFMAN, K?/AU
L14 0 L9 AND HOFFMAN, K?/AU

=> d l11, ibib abs fhitr, 1-16

L11 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

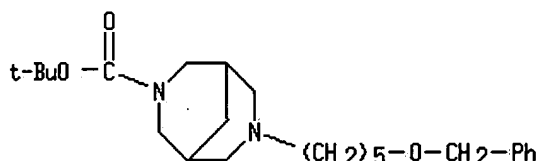
Full Text	Citing References
ACCESSION NUMBER:	2003:627083 HCAPLUS
DOCUMENT NUMBER:	139:307565
TITLE:	New solution free and polymer anchored chiral bispidine-based amino alcohols. Synthesis and screening for the enantioselective addition of diethylzinc to benzaldehyde
AUTHOR(S):	Lesma, Giordano; Danieli, Bruno; Passarella, Daniele; Sacchetti, Alessandro; Silvani, Alessandra
CORPORATE SOURCE:	Dipartimento di Chimica Organica e Industriale e Centro Interdisciplinare Studi biomolecolari e applicazioni Industriali (CISI), Universita degli Studi di Milano, Milan, 20133, Italy
SOURCE:	Tetrahedron: Asymmetry (2003), 14(16), 2453-2458 CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER:	Elsevier Science B.V.
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 139:307565
AB	A new approach was evaluated for the prepn. of soln. free and polymer-supported chiral bicyclic amino alcs. This strategy involves the use of readily available starting materials and allows chiral ligands characterized by the bispidine core, bearing a stereogenic center β to one of the nitrogen atoms to be obtained. The first results obtained from the application of these ligands in the asym. addn. reaction of diethylzinc to benzaldehyde are discussed.

IT 612092-88-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and reaction with chiral epoxides)

RN 612092-88-3 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[5-
(phenylmethoxy)pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2003:541859 HCAPLUS

DOCUMENT NUMBER: 140:31575

TITLE: Evaluation of generic chiral liquid chromatography
screens for pharmaceutical analysis

AUTHOR(S): Andersson, Margareta E.; Aslan, David; Clarke, Adrian;
Roeraade, Johan; Hagman, Gunnar

CORPORATE SOURCE: Department of Analytical Chemistry, AstraZeneca,
Soedertaelje, SE-151 85, Swed.

SOURCE: Journal of Chromatography, A (2003), 1005(1-2), 83-101
CODEN: JCRAEY; ISSN: 0021-9673

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

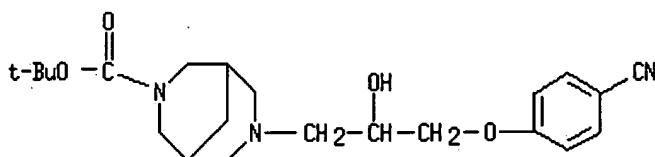
AB Two different automated generic liq. chromatog. screens for the sepn. of
chiral compds. of pharmaceutical interest were evaluated. The test set
comprised 53 chem. diverse chiral compds. involving 55 enantiomeric pairs
from the pharmaceutical industry (i.e. starting materials, synthetic
intermediates and drug substances). The first screen utilized four
polysaccharide-based columns with five mobile phases and showed
enantioselectivity for 87% of the test compds. The second screen employed
three macrocyclic glycopeptide columns with two mobile phases and showed
enantioselectivity for 65% of the test compds. Merging of the two
screening procedures resulted in an enantioselectivity for 96% of the
chiral compds. It is anticipated that the systematic use of the automated
chiral HPLC screens described in this report will substantially reduce the
necessary time for method development of pharmaceutically related chiral
anal. methods.

IT 227939-99-3

RL: ANT (Analyte); ANST (Analytical study)
(resoln. of drugs by liq. chromatog. using polysaccharide-based
columns)

RN 227939-99-3 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[3-(4-cyanophenoxy)-2-
hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

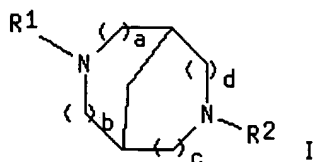
Full Text Citing
References

ACCESSION NUMBER: 2002:927433 HCAPLUS
DOCUMENT NUMBER: 138:14081
TITLE: Preparation of heteroaryl diazabicycloalkanes as central nervous system modulators
INVENTOR(S): Peters, Dan; Olsen, Gunnar M.; Nielsen, Elsebet Ostergaard; Ahring, Philip K.; Jorgensen, Tino Dyhring; Sloek, Frank Abildgaard
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096911	A1	20021205	WO 2002-DK347	20020523
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1397365	A1	20040317	EP 2002-724151	20020523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: DK 2001-866 A 20010601
WO 2002-DK347 W 20020523

OTHER SOURCE(S): MARPAT 138:14081
GI



AB The present invention relates to novel diazabicycloalkanes (shown as I; a/b/c/d = 1,1,1,1, 1,1,1,2, 1,1,2,1, 0,2,0,2 and 0,0,2,2; see below for addnl. definitions of variables; e.g. 3-benzyl-7-(6-phenyl-3-pyridazinyl)-3,7-diazabicyclo[3.3.1]nonane), their labeled or unlabeled forms, any of their enantiomers, any mixt. of enantiomers, or pharmaceutically

acceptable salts thereof or a prodrug thereof, which are cholinergic ligands at the nicotinic acetylcholine receptors and modulators of the monoamine receptors and transporters. Due to their pharmacol. profile the compds. of the invention may be useful for the treatment of diseases or disorders as diverse as those related to the cholinergic system of the central nervous system (CNS), the peripheral nervous system (PNS), diseases or disorders related to smooth muscle contraction, endocrine diseases or disorders, diseases or disorders related to neuro-degeneration, diseases or disorders related to inflammation, pain, and withdrawal symptoms caused by the termination of abuse of chem. substances. A diazabicycloalkane deriv. = those represented by Formula I, by Formula II, by Formula III, by Formula IV, and by Formula V. For I: n = 1, 2 or 3; R1 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkenylalkyl, alkynyl, alkynylalkyl, aryl, aralkyl or fluorescent group, which aryl groups may be substituted ≥ 1 times with substituents alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, methylenedioxy, hydroxy, alkoxy, alkoxyalkyl, alkoxyalkoxy, aryloxy, sulfhydryl, thioalkoxy, alkylcarbonyloxy, halogen, CF₃, OCF₃, CN, and nitro; and/or which aryl groups may be substituted with ≥ 1 fluorescent groups. R2 = a mono- or polycyclic aryl group, or a mono- or poly-heterocyclic group, which aryl and heterocyclic groups may be substituted ≥ 1 times with substituents alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, methylenedioxy, hydroxy, alkoxy, alkoxyalkyl, alkoxyalkoxy, aryloxy, sulfhydryl, thioalkoxy, alkylcarbonyloxy, halogen, CF₃, OCF₃, CN, and nitro; or which heterocyclic group may be substituted once with another mono- or poly-heterocyclic group, a mono- or polycyclic aryl group, or a mono- or polycyclic aralkyl group; and/or which heterocyclic group may be substituted with ≥ 1 fluorescent groups. Although the methods of prepn. are not claimed, several example preps. of I and intermediates are included and about 20 I are listed in the claims. Results for tabulated for two I regarding in vitro inhibition of 3H-5-Hydroxytryptamine (3H-5-HT, serotonin) uptake in cortical synaptosomes (e.g. IC₅₀ = 0.022 μ M for 3-benzyl-7-(2-quinolinyl)-3,7-diazabicyclo[3.3.1]nonane) and in vitro inhibition of 3H-cytisine binding (e.g. IC₅₀ = 0.0030 for 7-(6-chloro-3-pyridazinyl)-3,7-diazabicyclo[3.3.1]nonane).

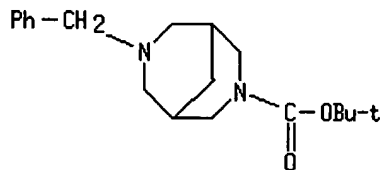
IT 227940-71-8P, 3-Benzyl-7-tert-butoxycarbonyl-3,7-diazabicyclo[3.3.1]nonane

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of heteroaryl diazabicycloalkanes as central nervous system modulators)

RN 227940-71-8 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

15

THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2002:840302 HCAPLUS
 DOCUMENT NUMBER: 138:255287
 TITLE: Solid-phase development of chiral phosphoramidite ligands for enantioselective conjugate addition reactions
 AUTHOR(S): Huttenloch, Oliver; Laxman, Eltepu; Waldmann, Herbert
 CORPORATE SOURCE: Max-Planck-Institut fur molekulare Physiologie
 Abteilung Chemische Biologie, Dortmund, 44227, Germany
 SOURCE: Chemistry--A European Journal (2002), 8(20), 4767-4780
 CODEN: CEUJED; ISSN: 0947-6539
 PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 138:255287

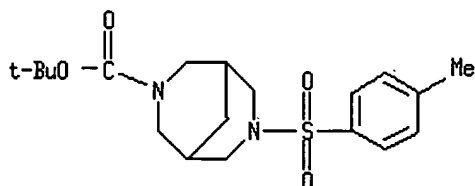
AB The development of a method for the optimization of chiral ligands for the steric steering of enantioselective Cu-catalyzed conjugate addns. of Zn-alkyls to enones is described. The method is based on combinatorial principles and solid-phase techniques. It includes the combinatorial synthesis of chiral bispidine-derived ligands embodying a phosphoramidite group on the solid phase and their study in immobilized form in the conjugate addn. of ZnEt₂ to cyclohexenone as test reaction. The best identified ligands were also synthesized sep. and studied in its sol. form. The results obtained for the polymer-bound ligands correctly mirrored the performance of the sol. ligands. The library embodied members giving ee values varying between 3 and 67%. The positional scanning approach proved to be invalid for the study of the ligand system, indicating that this approach in general should be applied with care. Taken together, the method allowed for rapid and efficient optimization of the ligands and led to the development of the 1st enantioselective, Cu-catalyzed conjugate addn. reaction with a polymer-bound ligand.

IT **454695-26-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. and cyclocondensation with phosphorus trichloride and binaphthol in the solid-phase development of chiral phosphoramidite ligands for enantioselective conjugate addn. reactions)

RN 454695-26-2 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[(4-methylphenyl)sulfonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



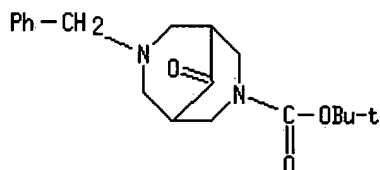
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2002:219731 HCAPLUS
 DOCUMENT NUMBER: 137:216696
 TITLE: Combinatorial development of chiral phosphoramidite-ligands for enantioselective conjugate addition reactions
 AUTHOR(S): Huttenloch, Oliver; Laxman, Eltepu; Waldmann, Herbert

CORPORATE SOURCE: Abteilung Chemische Biologie, Max-Planck-Institut fuer
molekulare Physiologie, Dortmund, 44227, Germany
SOURCE: Chemical Communications (Cambridge, United Kingdom)
(2002), (7), 673-675
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:216696
AB Chiral phosphoramidite ligands embodying bispidine frame work and a
binaphthyl phosphoramidite for Cu-catalyzed enantioselective conjugate
addn. reactions were developed employing principles of combinatorial and
solid phase chem.
IT 227940-70-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(combinatorial development of chiral phosphoramidite-ligands for
enantioselective conjugate addn. reactions)
RN 227940-70-7 HCAPLUS
CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 9-oxo-7-(phenylmethyl)-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2002:51458 HCAPLUS
DOCUMENT NUMBER: 136:118479
TITLE: Preparation of new bispidine compounds for the
treatment of cardiac arrhythmias
INVENTOR(S): Andersson, Kjell; Bjoere, Annika; Bjoersne, Magnus;
Ponten, Fritiof; Strandlund, Gert; Svensson, Peder;
Tottie, Louise
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 2002004446</u>	A1	20020117	<u>WO 2001-SE1544</u>	20010704
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,			

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1301510 A1 20030416 EP 2001-950132 20010704

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

BR 2001012267 A 20030520 BR 2001-12267 20010704

JP 2004502772 T2 20040129 JP 2002-509311 20010704

NO 2003000057 A 20030131 NO 2003-57 20030106

US 2003212095 A1 20031113 US 2003-332103 20030514

PRIORITY APPLN. INFO.:

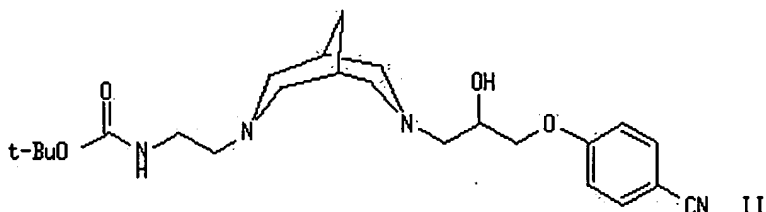
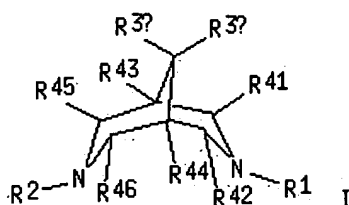
SE 2000-2603 A 20000707

SE 2000-2788 A 20000727

WO 2001-SE1544 W 20010704

OTHER SOURCE(S): MARPAT 136:118479

GI



AB The title compds. [I; R1 = ACR4R5BR6 (wherein R4 = H, halo, alkyl, etc.; or R4, together with R5, = O; R5 = H, alkyl,; A = a bond, alkylene, etc.; B = a bond, alkylene, etc.; R6 = (un)substituted aryl, 5-12 membered heterocyclyl contg. one or more heteroatoms selected from O, N and/or S); R2 = CN, (un)substituted 5-12 membered heterocyclyl contg. one or more heteroatoms selected from O, N and/or S, etc.; R3a, R3b = H, alkyl, etc.; or R3a and R3b together = alkylene, O(alkylene)O, etc.; R41-R46 = H, alkyl] which are useful in the prophylaxis and in the treatment of arrhythmias, in particular atrial and ventricular arrhythmias, were prepd. E.g., a 3-step synthesis of II was given. The exemplified compds. I showed pIC50 of at least 5.5 in glucocorticoid-treated mouse fibroblasts as a model to detect blockers of the delayed rectifier K current.

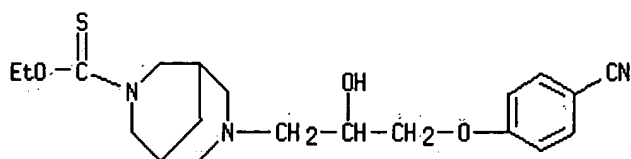
IT 389886-85-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of new bispidine compds. for the treatment of cardiac arrhythmias)

RN 389886-85-5 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carbothioic acid, 7-[3-(4-cyanophenoxy)-2-hydroxypropyl]-, O-ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2001:74816 HCAPLUS

DOCUMENT NUMBER: 134:320683

TITLE: Potassium and calcium current blocking properties of the novel antiarrhythmic agent H 345/52: implications for proarrhythmic potential

AUTHOR(S): Amos, G. J.; Abrahamsson, C.; Duker, G.; Hondeghem, L.; Palmer, M.; Carlsson, L.

CORPORATE SOURCE: AstraZeneca Research & Development Molndal, Integrative Pharmacology, Moelndal, S-43183, Swed.

SOURCE: Cardiovascular Research (2001), 49(2), 351-360
CODEN: CVREAU; ISSN: 0008-6363

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Objectives: To study the blocking effects of H 345/52 on ionic currents of rabbit ventricular myocytes and how these features translate into a proarrhythmic potential. Methods: The single electrode voltage clamp technique was used to study the effects of H 345/52 on the rapid component of the delayed rectifying potassium current, I_{Kr} , and the L-type calcium current (I_{Ca}). Differential effects of H 345/52 and almokalant on APD prolongation were studied in a rabbit Purkinje fiber/ventricular muscle prepn. The temporal variability of the action potential duration (APD) and its relation to proarrhythmias was examd. in Langendorff-perfused rabbit hearts administered H 345/52 or almokalant. Anesthetized, methoxamine-sensitized rabbits were used to assess the propensity of i.v. H 345/52 and ibutilide to induce torsades de pointes (TdP). Results: H 345/52 potently blocked I_{Kr} ($IC_{50}=40$ nM) without consequential use-dependency. The I_{Ca} was also blocked, but at higher concns. ($IC_{50}=1.3$ μ M). Block of I_{Ca} was markedly frequency-dependent (pos.) and influenced by membrane potential, such that H 345/52 was more effective following clamp steps from plateau potentials than from -80 mV. In the Purkinje fiber-ventricular muscle prepn., almokalant prolonged the Purkinje fiber APD preferentially, whereas H 345/52 homogeneously prolonged APD in both tissue types. In the perfused rabbit heart, H 345/52 (1 μ M) and almokalant (0.3 μ M) prolonged APD to a similar degree but increased the temporal variability of APD differently, from 3 ± 0.4 ms in control hearts to 8 ± 1.2 ms and to 38 ± 7.5 ms ($P<0.001$ vs. H 345/52), resp. Unequivocal early after-depolarizations were seen in 5/6 almokalant-perfused hearts but in no heart administered H 345/52 ($P<0.05$). In anesthetized rabbits, H 345/52 (17.4 μ mol/kg) or ibutilide (2.6 μ mol/kg max.), maximally lengthened the QT interval from 133 ± 4.5 to 177 ± 8.0 ms and from 125 ± 5.1 to 166 ± 9.3 ms ($P<0.001$, $n=8$). However, whereas ibutilide induced TdP in all animals at 0.06 ± 0.009 μ mol/kg, H 345/52 did not induce TdP ($P=0.0002$) at up to 17.4 μ mol/kg. Conclusions: H 345/52 blocks I_{Kr} with high potency and I_{Ca} with somewhat lower potency and was found to delay ventricular repolarization without substantially increasing temporal or spatial

dispersion and without inducing early after-depolarizations or TdP.

IT 227940-00-3, H 345/52

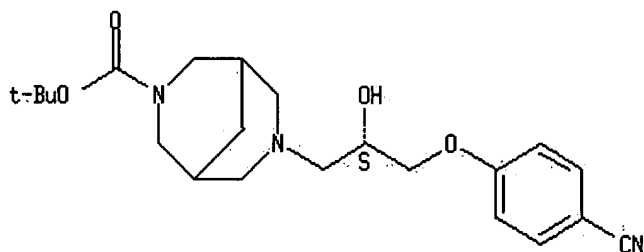
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(novel antiarrhythmic H 345/52: potassium and calcium current blocking properties and proarrhythmic potential)

RN 227940-00-3 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[(2S)-3-(4-cyanophenoxy)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2000:900634 HCAPLUS

DOCUMENT NUMBER: 134:42149

TITLE: Preparation of new bispidines useful in the treatment of cardiac arrhythmias

INVENTOR(S): Frantsi, Marianne; Hoffmann, Kurt-Jurgen; Strandlund, Gert

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076997	A1	20001221	WO 2000-SE1251	20000615
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000011675	A	20020319	BR 2000-11675	20000615
EP 1192155	A1	20020403	EP 2000-946587	20000615
EP 1192155	B1	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

JP 2003502326	T2	20030121	JP 2001-503855	20000615
EE 200100678	A	20030217	EE 2001-678	20000615
AT 236159	E	20030415	AT 2000-946587	20000615
NZ 516016	A	20030630	NZ 2000-516016	20000615
US 6465481	B1	20021015	US 2000-623707	20000907
ZA 2001009858	A	20030228	ZA 2001-9858	20011129
NO 2001006119	A	20020211	NO 2001-6119	20011214

PRIORITY APPLN. INFO.:

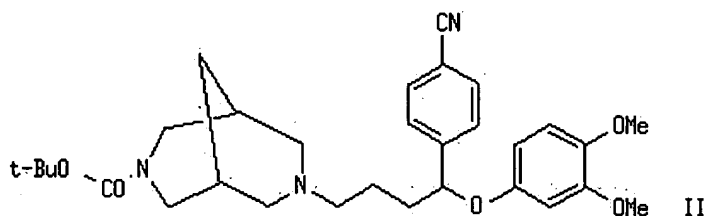
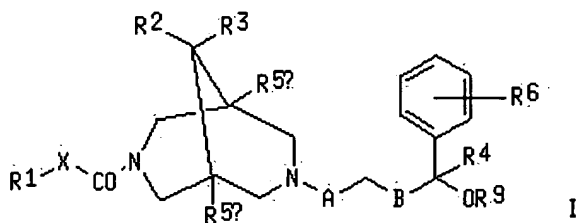
SE 1999-2271 A 19990616

WO 2000-SE1251 W 20000615

OTHER SOURCE(S):

CASREACT 134:42149; MARPAT 134:42149

GI



AB Bispidines, such as I [R1 = alkyl, arylalkyl, etc.; R2, R3, R4, R5a, R5b = H, alkyl; R6 = OH, CN, NO2, NH2, halogen, etc.; R9 = alkyl, aryl, acyl, etc.; X = O, S; A, B = bond, linking group, such as alkylene, etc.], were prepd. for pharmaceutical use in the treatment of cardiac arrhythmias, in particular atrial and ventricular arrhythmias. Thus, bispidine II was prepd. in multistep synthetic sequence starting from N,N'-dibenzylbispidine, 4-(1-hydroxy-3-butenyl)benzonitrile, and 3,4-dimethoxyphenol. The prepd. bispidines were tested for primary electrophysiol. effects in anesthetized guinea pigs.

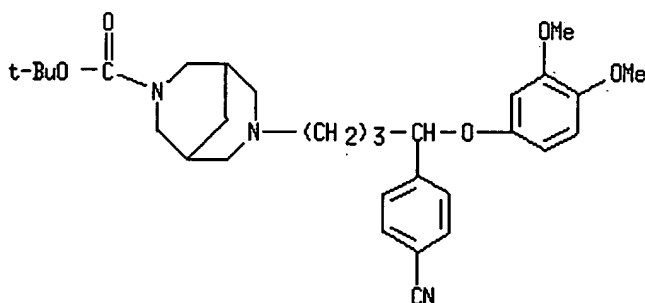
IT **312955-28-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of bispidines useful in the treatment of cardiac arrhythmias)

RN **312955-28-5** HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[4-(4-cyanophenyl)-4-(3,4-dimethoxyphenoxy)butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2000:528839 HCAPLUS
 DOCUMENT NUMBER: 133:281937
 TITLE: Diastereoselective synthesis of sparteine analogues via lithiation-electrophilic quench of N-Boc bispidines
 AUTHOR(S): Harrison, J. R.; O'Brien, P.
 CORPORATE SOURCE: Department of Chemistry, University of York, Heslington, York, YO10 5DD, UK
 SOURCE: Tetrahedron Letters (2000), 41(32), 6161-6165
 CODEN: TELEAY; ISSN: 0040-4039
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 133:281937

AB Lithiation of a N-Boc bispidine and subsequent trapping with a range of electrophiles has been investigated as a new route to sparteine analogs. The reactions proceed with complete diastereoselectivity to generate products with the same relative stereochem. as in the ABC rings of sparteine.

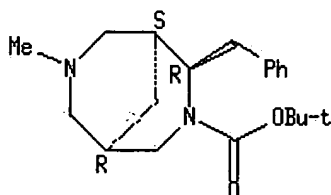
IT 299914-51-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (diastereoselective synthesis of sparteine analogs from N-Boc bispidines)

RN 299914-51-5 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-methyl-2-(phenylmethyl)-, 1,1-dimethylethyl ester, (1R,2S,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

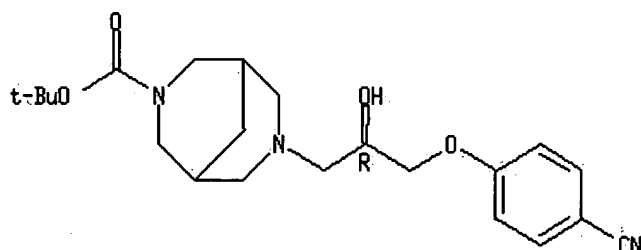
L11 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2000:260016 HCAPLUS
 DOCUMENT NUMBER: 132:284247
 TITLE: A dried or frozen pharmaceutical preparation containing a class III antiarrhythmic compound
 INVENTOR(S): Bjore, Annika; Granath, Anna-Karin
 PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
 SOURCE: PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 2000021533</u>	A1	20000420	<u>WO 1999-SE1828</u>	19991011
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
<u>CA 2315375</u>	AA	20000420	<u>CA 1999-2315375</u>	19991011
<u>BR 9906869</u>	A	20001017	<u>BR 1999-6869</u>	19991011
<u>EP 1043997</u>	A1	20001018	<u>EP 1999-970322</u>	19991011
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
<u>EE 200000354</u>	A	20011217	<u>EE 2000-354</u>	19991011
<u>JP 2002527394</u>	T2	20020827	<u>JP 2000-575509</u>	19991011
<u>US 6492382</u>	B1	20021210	<u>US 1999-423200</u>	19991103
<u>ZA 2000002749</u>	A	20010111	<u>ZA 2000-2749</u>	20000601
<u>NO 2000002986</u>	A	20000609	<u>NO 2000-2986</u>	20000609
PRIORITY APPLN. INFO.:			<u>SE 1998-3517</u>	A 19981015
			<u>WO 1999-SE1828</u>	W 19991011
OTHER SOURCE(S): MARPAT 132:284247				
AB	The present invention relates to dried prepns. contg. a class III antiarrhythmic compd. in the form of cryst. or amorphous salt or any combination thereof, where the counterion is selected from pharmaceutically acceptable water-sol. org. or inorg. acids. The present invention also relates to frozen prepns. contg. a class III antiarrhythmic compd. in the form of salt soln., where the counterion is selected from pharmaceutically acceptable water-sol. org. or inorg. acids. Preferred prepns. contain a salt of the compd. 3,7-diazabicyclo[3.3.1]-nonane-3-carboxylic acid 7-[(2S)-3-(4-cyanophenoxy)-2-hydroxypropyl]-1,1-dimethylethyl ester (Compd. A). Further aspects of the present invention include salts of Compd. A per se, processes for prepg. the prepn., as well as use of the prepns. for prophylaxis and/or treatment of cardiac arrhythmia.			
IT	<u>227940-01-4</u>			
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)			
	(freeze-dried pharmaceuticals contg. antiarrhythmic diazabicyclononanecarboxylate deriv.)			
RN	<u>227940-01-4</u> HCAPLUS			
CN	3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[(2R)-3-(4-cyanophenoxy)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)			

Absolute stereochemistry.

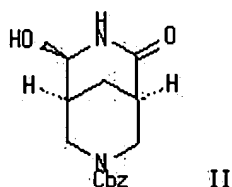
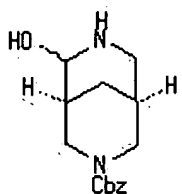


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:	1999:631969 HCAPLUS
DOCUMENT NUMBER:	132:12427
TITLE:	An efficient chemoenzymatic access to chiral 3,7-diazabicyclo[3.3.1]nonane derivatives
AUTHOR(S):	Danieli, Bruno; Lesma, Giordano; Passarella, Daniele; Silvani, Alessandra; Viviani, Nunzia
CORPORATE SOURCE:	Dipartimento di Chimica Organica e Industriale, Universita degli Studi di Milano, Centro CNR di Studio per le Sostanze Organiche Naturali, Milan, 21-20133, Italy
SOURCE:	Tetrahedron (1999), 55(40), 11871-11878 CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER:	Elsevier Science Ltd.
DOCUMENT TYPE:	Journal
LANGUAGE:	English
GI	



AB Enantiopure 3,7-diazabicyclo[3.3.1]nonane derivs. I and II, potential precursors of quinolizidine alkaloids, were synthesized in high yields, starting from the biocatalytic asymmetric reduction of σ -sym. 3,5-disubstituted piperidines. Their application to the total synthesis of the new pharmacol. active compds. are also described.

IT **251346-88-0P**

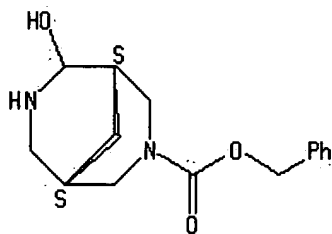
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(chemoenzymic access to chiral 3,7-diazabicyclo[3.3.1]nonane derivs.)

RN **251346-88-0** HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 6-hydroxy-, phenylmethyl ester, (1S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

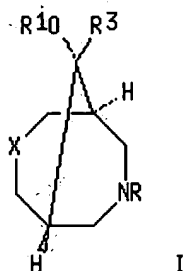
Full Text	Citing References
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ACCESSION NUMBER: 1999:421688 HCAPLUS
DOCUMENT NUMBER: 131:58813
TITLE: Preparation of bicyclic nitrogen compounds as Kv2.1 antagonists
INVENTOR(S): Bubacz, Dulce Garrido; Dukes, Iain David; McLean, Ed Williams; Noe, Robert Anderson; Peat, Andrew James; Szewczyk, Jerzy Ryszard; Thomson, Stephen Andrew; Worley, Jennings Franklin, III
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932487	A1	19990701	WO 1998-EP8085	19981216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9919671	A1	19990712	AU 1999-19671	19981216
EP 1042322	A1	20001011	EP 1998-964497	19981216
EP 1042322	B1	20020417		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001526289	T2	20011218	JP 2000-525424	19981216
AT 216386	E	20020515	AT 1998-964497	19981216
ES 2175842	T3	20021116	ES 1998-964497	19981216
US 6589934	B1	20030708	US 2000-581386	20000613

PRIORITY APPLN. INFO.: GB 1997-26630 A 19971218
WO 1998-EP8085 W 19981216

OTHER SOURCE(S): MARPAT 131:58813
GI



AB Treatment of non-insulin dependent diabetes mellitus, i.e., administration of antagonists I [R = alkyl, alkenyl, alkoxyalkyl, etc.; R1 = substituted benzyl, substituted benzoyl, etc.; X = S, O, NR2; R3 = H, alkyl] of the delayed rectifier potassium channel Kv2.1, is reported. E.g., anti-3-(4-(3,4-methylenedioxyphenyl)butyl)-7-methyl-3,7-diazabicyclononan-9-ol 4-chlorobenzoate was prepd.

IT **228270-21-1P**

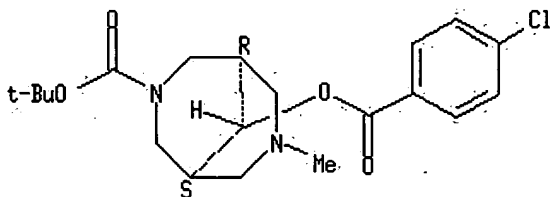
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of bicyclic nitrogen compds. as Kv2.1 antagonists)

RN **228270-21-1** HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 9-[(4-chlorobenzoyl)oxy]-7-methyl-, 1,1-dimethylethyl ester, (9-anti)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT:

7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1998:53390 HCAPLUS

DOCUMENT NUMBER: 128:180115

TITLE: Stereochemistry of N-acetyl-r-2,c-4-diphenyl-3-azabicyclo[3.3.1]nonanes and N-ethoxycarbonyl-r-2,c-4-diphenyl-3-azabicyclo[3.3.1]nonane

AUTHOR(S): Jeyaraman, R.; Ponnuswamy, S.

CORPORATE SOURCE: Department of Chemistry, Bharathidasan University, Tiruchirapalli, 620 024, India

SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1997), 36B(9), 730-737

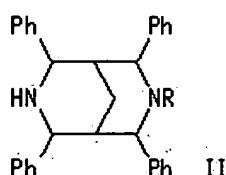
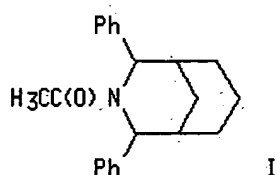
CODEN: IJSBDB; ISSN: 0376-4699

PUBLISHER: National Institute of Science Communication, CSIR

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB The conformational preferences of N-acetyl-r-2,c-4-diphenyl-3-azabicyclo[3.3.1] nonane I and N-ethoxycarbonyl- and N-acetyl-r-2,c-4,t-6,t-8-tetraphenyl-3,7-diazabicyclo[3.3.1] nonanes II (R= CO₂Et, COMe) have been studied using NMR spectral techniques. The azabicyclo[3.3.1]nonane I is found to prefer a twin-chair conformation with a slight flattening at the nitrogen end. In the case of diazabicycles II both the ethoxycarbonylation and acetylation reactions are found to take place only at the boat end of the parent amine and the preferred conformation of the products is found to be twin-chair with flattening at C1-C2-N3-C4-C5 part of the ring in both cases. The energy barrier for the N-CO rotation in N-ethoxycarbonyl deriv. 6 has been detd. from the dynamic ¹H NMR studies and the barrier for N-CO rotation is found to be 50.8 kJ mol⁻¹, much less than that of N-nitroso analogs.

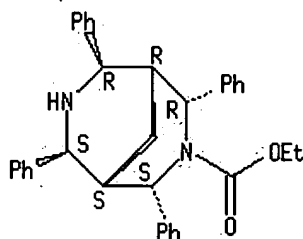
IT **203190-52-7P**, N-(Ethoxycarbonyl)-r-2,c-4-diphenyl-3-azabicyclo[3.3.1]nonane

RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(dynamic NMR conformational anal. of ethoxycarbonyl- and acetyltetraphenyldiazabicyclononanes)

RN **203190-52-7** HCAPLUS

CN **3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 2,4,6,8-tetraphenyl-, ethyl ester, (2R,4S,6S,8R)-rel-[partial]- (9CI) (CA INDEX NAME)**

Relative stereochemistry.



REFERENCE COUNT:

39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1995:441037 HCAPLUS

DOCUMENT NUMBER: 123:111879

TITLE: Synthesis and biological activity of the metabolites of syn-3-ethyl-7-methyl-3,7-diazabicyclo[3.3.1]non-9-yl 4-chlorobenzoate hydrochloride

AUTHOR(S): Yamawaki, Ichiro; Bukovac, Scott W.; Sunami, Akihiko
CORPORATE SOURCE: Tokushima Res. Cent., Pharmacokinetics Res. Lab. and Pharmacol. Res. Lab., Tokushima, 771-01, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (1994), 42(11), 2365-9

PUBLISHER: CODEN: CPBTAL; ISSN: 0009-2363
Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 123:111879

AB Five metabolites of syn-3-ethyl-7-methyl-3,7-diazabicyclo[3.3.1]non-9-yl 4-chlorobenzoate hydrochloride (YUTAC) were prepd. and examd. for Na⁺ current blocking activity in guinea pig ventricular myocytes. These metabolites showed lower inhibitory activities than the parent compd. or were inactive.

IT 166272-89-5P

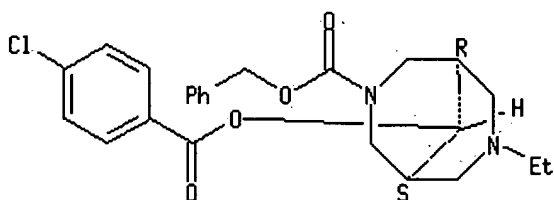
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and Na⁺ current blocking activity of the metabolites of Yutac)

RN 166272-89-5 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3-carboxylic acid, 9-[(4-chlorobenzoyl)oxy]-7-ethyl-, phenylmethyl ester, syn- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L11 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1982:104172 HCAPLUS

DOCUMENT NUMBER: 96:104172

TITLE: Synthesis and reactions of polyhedral compounds. II. Synthesis of 5,7-dimethyl-1,3-diazaadamantan-6-one and -6-ol and their conversion into 3,7-diacyl(dicarbalkoxy, diarylsulfonyl)-3,7-diazabicyclo[3,3,1]nonanes

AUTHOR(S): Agadzhanyan, Ts. E.; Arutyunyan, G. L.

CORPORATE SOURCE: Inst. Tonkoi Org. Khim. im. Mndzhoyana, Yerevan, USSR

SOURCE: Armyanskii Khimicheskii Zhurnal (1981), 34(11), 963-8

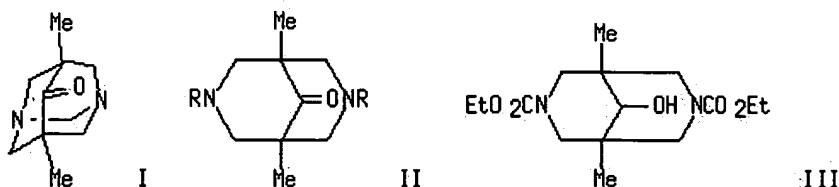
CODEN: AYKZAN; ISSN: 0515-9628

DOCUMENT TYPE: Journal

LANGUAGE: Russian

OTHER SOURCE(S): CASREACT 96:104172

GI



AB Cyclocondensation of EtCOEt, HCHO, and AcONH₄ gave 19.5% I, which reacted with RCOCl, RO₂CCl, or ArSO₂Cl to give II [R = BrCH₂CO, BrCH₂CH₂CO, CH₂:CHCO, Bz, (phthalimidomethoxy)carbonyl, EtOCO, PhCH₂OCO, 4-MeC₆H₄SO₂, 4-(MeO₂CNH)C₆H₄SO₂]. LiAlH₄ redn. of I gave 83.3% alc., which with ClCO₂Et gave III.

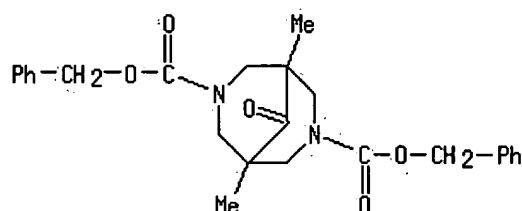
IT 80808-93-1P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

RN 80808-93-1 HCAPLUS

CN 3,7-Diazabicyclo[3.3.1]nonane-3,7-dicarboxylic acid, 1,5-dimethyl-9-oxo-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



L11 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1958:40589 HCAPLUS
 DOCUMENT NUMBER: 52:40589
 ORIGINAL REFERENCE NO.: 52:7312e-i,7313a-f
 TITLE: Compounds with urotropine structure. IX. Bispidine
 AUTHOR(S): Stetter, Hermann; Merten, Rudolf
 CORPORATE SOURCE: Univ. Munich, Germany
 SOURCE: Chemische Berichte (1957), 90, 868-75
 CODEN: CHBEAM; ISSN: 0009-2940

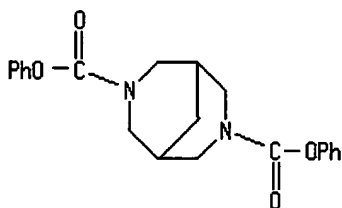
DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 OTHER SOURCE(S): CASREACT 52:40589

GI For diagram(s), see printed CA Issue.

AB cf. C.A. 51, 7309i. The previously described (C.A. 50, 7815c) synthesis of bispidine (I) was simplified and the yield improved. Since it was found that both cis and trans configurations of the diamide (II) of N-tosylpiperidine-3,5-dicarboxylic acid (III) cyclized to 2,4-dioxo-7-tosylbispidine (IV) with equal ease (the trans changed to the cis isomer under the conditions of ring closure), the wasteful sepn. of the isomers became unnecessary. Therefore, 50 g. crude III refluxed with 80 cc. SOCl₂, warmed slowly to boiling on an H₂O bath, boiled 6-8 hrs. until no more HCl evolved, kept overnight, excess SOCl₂ removed in vacuo, the residual acid chloride in 100 cc. C₆H₆ added dropwise (15 min.) under ice cooling to 150 cc. concd. NH₄OH and 125 g. ice, and stirred 1-2 hrs. at room temp. yielded 85-90% crude II, m. 245-50°, and this cyclized as before (loc. cit.) in 700 cc. 1-MeClOH₇ yielded 80% IV. Or 35 g. crude III evapd. in vacuo with 150 cc. concd. NH₄OH, the sirupy residue in 500 cc. 1-MeClOH₇ stirred about 8 hrs. at 130-50°, while the resulting H₂O distd. and NH₃ passed through the mixt., heated an addnl. 3 hrs. to boiling, and stirred another 4 hrs. at 250° yielded 77% IV. Although the 2nd method seemed more direct, the product was less pure and the yield less. Reduction of IV with LiAlH₄ as before (loc. cit.) gave I, purified in vacuo, b₁ 154-6°, b₉ 190-5°. Crude I (2 g.) in 10 cc. C₆H₆ treated under ice cooling with 10 cc. Ac₂O in 5 cc. C₆H₆, heated 3 hrs. on an H₂O bath, kept overnight, the solvents evapd., 30 cc. H₂O added to the residue, and the filtrate from the resulting solid concd. in vacuo yielded 60% N,N'-Ac₂ deriv. of I, m. 163° (1:1 ligroine-C₆H₆). I (0.5 g.) refluxed 8 hrs. with 2 cc. BzCl and 4 g. K₂CO₃ in 50 cc. C₆H₆ gave N,N'-Bz₂ deriv. of I, m. 233-5° (1:1 ligroine-C₆H₆). I (0.5 g.) in 10 cc. H₂O neutralized with dil. HCl, 2 g. NaNO₂ in 15 cc. H₂O and 1 cc. N HCl added, the mixt. warmed 3 hrs. on an H₂O bath, evapd. to half vol., and satd. with solid K₂CO₃ gave the N,N'-(NO)₂ deriv. of I, m. 268.5-9.0° (decompn.) (MePh), formed also by the same treatment of 1,3-diazaadamantane (V) (loc. cit.) in place

of I, with the splitting off of CH_2O . A similar splitting off of CH_2O took place upon treatment of V with p-MeC₆H₄SO₂Cl (VI) to yield 83% N,N'-ditosyl deriv. of I, formed also from I with VI. I. (1.6 g.) heated 2 hrs. to 165° with 2.75 g. Ph_2CO_3 , an addnl. 3 hrs. at 165-75°, cooled, and extd. with CHCl_3 yielded 40% N,N'-(CO₂Ph)₂ deriv. of I, m. 172.5-4° (ligroine). I (0.6 g.) heated with 0.47 g. sulfamide 2 hrs. at 115° and then 4 hrs. at 135° until no more NH_3 was evolved yielded on cooling 70-5% N,N'-(SO₂NH₂)₂ deriv. of I, m. 229-31° (H_2O). Thus, attempted cyclization of I to derivs. of V by such reagents resulted only in open-chain derivs. of I, and these failures were ascribed to steric strain in fitting the CO or SO groups into the ring system of V. However, since the valence angle of S is only slightly different from the tetrahedral angle, 4.5 g. I in 35 cc. abs. EtOH treated with 6.7 g. (EtO)₂S in 25 cc. abs. EtOH, warmed slowly to boiling on a H_2O bath, refluxed 3 hrs. (moisture excluded), kept overnight, the filtrate from S concd. in vacuo, and cooled to 0° yielded 2.5-2.8 g. 2-thia-1,3-diazaadamantane (VII), m. 160° (decompn.) (purified by sublimation). VII showed the volatility characteristic of compds. with urotropine structure, was unstable toward aq. acids and alkalis, and decompd. on attempted oxidation of the S to the SO group. A new type of compd. with urotropine structure was formed as a complex salt of I with Cu or Ni as the central atom. I (2 g.) and 0.8 g. (AcO)₂Cu in 300 cc. H_2O warmed with active C, filtered, and the filtrate evapd. to dryness gave VIII (M = Cu, X = AcO), m. 140-1° (decompn.). Similarly, 1.1 g. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ with 1.3 g. I in 150 cc. H_2O gave VIII (M = Ni, X = Cl), yellow needles, changing to red-yellow at 60°, red at 270°, and sintering at 325° to a green mass. The dissocn. consts. of both VIII were detd. by the polarographic method of Laitinen, et al. (C.A. 43, 6933a), as 2.96×10^{-21} and 1.66×10^{-17} for the Cu and Ni complexes, resp., showing the stability of the Cu complex to be about 10 times the stability of $[\text{Cu}(\text{en})_2]^{++}$. The failure of Ag, Zn, Cd, Co, Cr, or Pd ions to form similar complexes with I was ascribed to the need to fit a central atom of quite definite vol. into the complex. This seems a remarkable case of selective complex formation, wherein the selectivity is governed by purely steric factors.

IT 102660-79-7, 3,7-Diazabicyclo[3.3.1]nonane-3,7-dicarboxylic acid, diphenyl ester
(prepn. of)
RN 102660-79-7 HCAPLUS
CN 3,7-Diazabicyclo[3.3.1]nonane-3,7-dicarboxylic acid, diphenyl ester (6CI)
(CA INDEX NAME)



=> file caold

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FILE 'REGISTRY' ENTERED AT 18:37:34 ON 31 MAR 2004

L1 STRUCTURE UPLOADED
 L2 50 S L1
 L3 2733 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 18:39:23 ON 31 MAR 2004

L4 86 S L3/THU
 L5 52 S L4 AND ?ARRHYTHM?

FILE 'REGISTRY' ENTERED AT 18:44:53 ON 31 MAR 2004

L6 STRUCTURE UPLOADED
 L7 8 S L6
 L8 142 S L6 FULL

FILE 'HCAPLUS' ENTERED AT 18:47:02 ON 31 MAR 2004

L9 20 S L8
 L10 4 S L9 AND BJORSNE, M?/AU
 L11 16 S L9 NOT L10
 L12 1 S L11 AND FRANTSI, M?/AU
 L13 1 S L12 NOT L10
 L14 0 S L9 AND HOFFMAN, K?/AU

FILE 'CAOLD' ENTERED AT 19:09:11 ON 31 MAR 2004

=> s l8

L15 1 L8

=> d l15, all, 1

L15 ANSWER 1 OF 1 CAOLD COPYRIGHT 2004 ACS on STN
 AN CA52:7312e CAOLD
 TI compds. with urotropine structure - (IX) bispidine
 AU Stetter, Hermann; Merten, R.
 IT 280-74-0 281-30-1 6711-35-9 98433-39-7 99669-80-4 101117-22-0
102660-79-7 110570-65-5 112948-63-7 128687-08-1 129067-62-5

=> fil reg; d acc 102660-79-7; fil CAOLD

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ANSWER 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 102660-79-7 REGISTRY

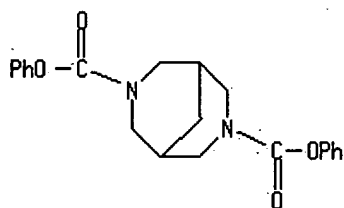
CN 3,7-Diazabicyclo[3.3.1]nonane-3,7-dicarboxylic acid, diphenyl ester (6CI)
(CA INDEX NAME)

FS 3D CONCORD

MF C21 H22 N2 O4

SR CAOLD

LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

FILE 'CAOLD' ENTERED AT 19:09:30 ON 31 MAR 2004

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
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